EXTRACTION OF THE GUINEA WORM

From an engraving by J. H. Jördens (1802)

HUMAN HELMINTHOLOGY

A MANUAL FOR PHYSICIANS, SANITARIANS AND MEDICAL ZOOLOGISTS

BY

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PREFACE TO THE THIRD EDITION

DURING the years which have elapsed since the second edition of this volume came from the press, a wealth of material has been published in the field of helminthology, including particularly the helminths which parasitize man. Many of the more significant findings have resulted from investigations conducted during military operations in warm climates between the years 1942 and 1945. This is illustrated by the numerous contributions made to the biology, epidemiology, pathogenesis, diagnosis, treatment and control of Bancrofts' filariasis and schistosomiasis japonica. An earlier revision of this book could not have included many of these contributions.

This edition of Human Helminthology constitutes a complete revision. New data and concepts have been introduced in generous amounts, while older information has been reëvaluated. It is hoped that this edition will be equally helpful to the physician, the sanitary officer and student of parasitology.

Sincere thanks are extended to many individuals who have made suggestions for improving the book. Special acknowledgement is made to Professor M. A. Stewart of the University of California for providing an up-to-date list of insects involved as intermediate hosts of helminths, to Professors Paul C. Beaver and G. M. Carrera of the Department of Tropical Medicine and Public Health, Tulane University, for valuable comments on the new glossary incorporated in Chapter I, and to Professor Beaver for a description of his new egg-count technic. Finally, the author expresses sincere gratitude to the publishers, Lea and Febiger, for sympathetic understanding during the period of publication of this edition.

ERNEST CARROLL FAUST

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PREFACE TO THE FIRST EDITION

As an investigator in the field of medical parasitology for nearly two decades and a teacher of the subject to physicians and zoölogists, the author has followed closely the important steps in the development of the subject. In no phase of medical zoölogy, both in its biological and its clinical aspects, has greater progress been made than in helminthology. Thus far, however, no attempt has been made to correlate the available information, much of which has been published in inaccessible journals, and to bring it together into a manual which would meet the needs of the parasitologist. The present volume is the result of the author's own need for a teaching and reference text on the subject. It is also significant that certain of the author's colleagues as well as many of his students have urged him to make available for them the subject matter of human helminthology. This has been no easy task, especially since the field includes both theoretical and practical problems. It is felt, however, that the form in which the data have been compiled will serve this two-fold end and will, furthermore, make the information available alike to the clinician, the sanitarian, and the medical zoölogist. Although each of these workers, from his peculiar vantage point, is primarily concerned with one particular aspect of the subject, he is also interested in the problem as a whole, and will appreciate the need for an all-around presentation of the available information in the field.

Of necessity the author has depended on the work of his colleagues for much of the evidence and many of the views expressed in this volume. Sincere thanks are here expressed to those who have either directly or indirectly contributed to the contents or form of the manual. The difficulties of obtaining adequate and well-balanced illustrations have been considerable. Those who have generously placed their original or published figures at the disposal of the author deserve no small share in whatever of credit may come from the adventure. Grateful thanks are also due to those who have assisted in typing the manuscript, in revising the proof and in compiling the index. Last, but not least, the courteous personal cooperation which the publishers, Messrs. Lea and Febiger, have provided, and the high ethical standards which they have consistently maintained during the five-year period of writing and of publishing the volume call for the highest praise.

ERNEST CARROLL FAUST

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HUMAN HELMINTHOLOGY

SECTION I

THE SCOPE OF HELMINTHOLOGY

CHAPTER I

THE PHENOMENON OF PARASITISM IN HELMINTH GROUPS

INTRODUCTION

Parasitism is the state whereby one organism lives on or in another organism, and thus derives benefit, without contributing to this association. Cameron (1940) refers to parasitism as "a mode of life" This phenomenon is not confined to the Animal Kingdom but is found in many groups of bacter
plants
many
and study from the earliest times. Those species of organisms which parasitize the human body and thereby bring about human disease are of special concern to the medical profession. However, in order that the student of medicine may have an intelligent comprehension of the strictly human parasites, it is essential that he view in brief the phenomenon of parasitism as a whole and the relationship of the species parasitic on or in the human body to the more inclusive subject of parasites as a physiological group.

First of all the parasite must be distinguished from the predacious organism. The *parasite* lives at the expense of another organism which harbors it and which is commonly called its *host*. If it is well adapted to the host, no appreciable harm results On the other hand the *predacious organism*, or *predator*, kills the animal which it attacks, either at once or piecemeal, in order to devour it. There are many gradations between the predacious animal and the well adapted parasite. Various names have been applied to those species which on the one hand, feed only upon the waste products of the host, and, on the other, are actually helpful to the host. The former are usually referred to as *commensals*, the latter, as *symbionts*. As an example of the former may be mentioned the common colon ameba of man, as an example of the latter, the intestinal flora which preserves a constant hydrogen-ion concentration and, indirectly at least, serves in the digestion of food and passage of water through the intestinal tract At times the giant intestinal roundworm, *Ascaris lumbricoides*, appears to be a harmless commensal; more frequently it is a dangerous parasite. Since it is of

great importance for the physician to know, wherever possible, the relative danger from infection with a particular organism found in the human body, an attempt will be made in the pages referring to individual species of parasites to evaluate the relative degrees of pathogenicity of these "guests" to their "hosts." While there is a wide variation existing all the way from the harmless commensal to the poorly adapted parasite which produces a diseased condition of the host, it is convenient to designate all of these types of parasites as *"guests,"* without reference to their degree of parasitism. The term "guest" is the more justifiable since certain species are at times entirely harmless and at other times "unwelcome" and actually dangerous to the life of the host.

Parasitism comprehends "host" and "guest" relationships in both the Animal and the Plant Kingdoms. A plant parasite (*phytoparasite*) may be parasitic on another plant, as, for example, the barberry rust (*Puccinia graminis*) on grain, or the dry rot (*Volutella fructi*) on the apple; or it may parasitize an animal host, as, for example, the fungi which produce the various mycoses of man, such as actinomycosis and Madura foot. Likewise, animal parasites (*zoöparasites*) may parasitize plants, as, for example, the thousands of species of insects which live upon or within plants of economic value to man; or they may be adapted to a life of parasitism in animals, as, for example, the hookworm in man. An interesting example whereby a zoöparasite utilizes a plant as an object on which to encyst, and thus may be transferred passively to man who consumes the vegetable in the raw state, is found in *Fasciolopsis*, the giant intestinal fluke. The object of such a transfer, which is purely mechanical, is referred to as a *mechanical vector* or agent, and differs from a *biological vector* which is essential in the life cycle of the parasite.

If an organism lives entirely on dead tissue or food, it is referred to, not as a parasite, but as a *saprobiont* or a *saprophage*. In case this waste consists of fecal material the organism is a *coprobiont* or a *coprophage*. If the organism in these instances is an animal species, it is designated in the first case as a *saprozoite* and in the second case as a *coprozoite*. Certain organisms which are accidentally *en transit* through the digestive tract and are diagnosed from examination of the stool are referred to as *fecal contaminators*. Such is the egg of the nematode species, *Heterodera marioni* (synonym *H. radicicola*), at times found in the fleshy roots of vegetables consumed by man and at one time incorrectly diagnosed from the superficial resemblance of its egg to that of *Enterobius vermicularis* as *"Oxyuris incognita."*

Some organisms which depend on others for food are entirely *ectoparasitic*. The feather lice of birds (Mallophaga) live entirely on the feathers and the filth accumulated among the plumage of their host. The sucking lice (Anoplura), fleas, bedbugs and blood-sucking Diptera are all ectoparasitic, but secure their nourishment from the blood of the host. Ectoparasitism is conveniently referred to as an *infestation*. Other organisms are *endoparasitic*, that is, parasitic within the host species. Those living free in the lumen of the intestine are not actual endoparasites but are popularly referred to as such. Those attached to the intestinal wall or even more intimately parasitic in the tissues of the host as, for example, the hookworm

or the human blood fluke, are true endoparasites. Endoparasitism is considered as an *infection*, whether the parasite be a bacterium, a spirochete, a filtrable virus, a protozoon or a helminth, *irrespective of the parasite's* proven ability to reproduce itself within the body of its host. Organisms which are able to live either a free or a parasitic existence are spoken of as *facultative parasites;* those which have become completely dependent on their host for existence are designated as *obligatory parasites.*

Parasites are most commonly found in three large divisions of the Animal Kingdom—the Protozoa, or one-celled organisms, the Helminths, or parasitic worms, and the Arthropods, or invertebrate species with [illegible] commonly referred to [illegible] λμινς). Originally the term "helminth" meant "intestinal worm," *but for many years the concept* has been more broadly interpreted. The term "helminth" does not connote a single group or phylum of the Animal Kingdom, but refers to two large phyla, the **Platyhelminthes**, or flatworms, and the **Nematoda** or roundworms, as well as to two small phyla, the **Acanthocephala**, or thorny-headed worms, and the **Nematomorpha**. In addition, one class group of the phylum Annelida, namely the **Hirudinea**, or leeches, are, in a somewhat broader sense, included within the definition of "helminths." These groups differ *from each other both in external appearance and in fundamental organization*: the flatworms have no body cavity and their digestive tract, when present, consists typically of one or two blind pouches; the roundworms (*sensu stricto*) have a body cavity although not lined with mesoderm, and a complete digestive tract with both oral and anal openings. The Acanthocephala have a body cavity and a proboscis typically armed with hooklets. The Nematomorpha have a body cavity lined with mesoderm and germaria discontinuous with their ducts The leeches, as distinct from all other helminths, have true metamerism. The flatworms are usually hermaphroditic (*i. e.*, monecious); the roundworms are usually diecious. A majority of the flatworms and a very large part of the roundworms have become *adapted to a parasitic existence; their reproductive products have become* disproportionately multiplied when compared with the majority of free-living species, thus ensuring a greater degree of certainty in propagation of their kind.

In the case of the **Platyhelminthes**, or flatworms, two of the four usually recognized classes, the **Trematoda**, or flukes, and the **Cestoidea**, or tapeworms, are exclusively parasitic, and the remaining two class groups, the **Turbellaria** and the **Nemertea**, consist almost exclusively of free-living *organisms. While there are thousands of species of parasitic* **Nematoda**, or roundworms, there are an even larger number of species of this phylum which are free-living forms The **Acanthocephala**, are exclusively parasitic. Among the **Nematomorpha** *the gordiid worms, or "hair snakes," are consistently* parasitic during their immature stages. The **Hirudinea** are blood suckers, and may be external (*Hæmadipsa* spp.), within the mouth and upper respiratory tract (*Limnatis nilotica*) or within the genito-urinary tract.

or around the oral end to assist in attachment. In the pork tapeworm (*Tænia solium*) these hooks are arranged as a crown on the rostellum, anterior to the sucking cups. In the dog tapeworm they occur in several rows around a proboscis-like organ at the anteriormost part of the body, which may be inverted or everted as the parasite requires. A similar arrangement is found at the anterior end of the head of the thorny-headed worm (*Macracanthorhynchus hirudinaceus*) commonly found in the pig, and rarely parasitic in man. The hookworm has a series of teeth or cutting plates just within its buccal capsule, which serve to attach the worm firmly to the mucosa of the host's intestine. *Ternidens deminutus* has a buccal armature of tooth-like structures directed anteriad, and serving both for tissue abrasion and for anchoring of the parasite.

In some of the helminths secretory glands have been developed in the vicinity of the mouth, which serve in establishing the worm in a favorable habitat, or aid in supplying food to the worm. In the trematodes these glands are most conspicuous in the miracidial and cercarial stages and serve the purpose of penetrating the outer tissues of the host. They consist of paired unicellular glands, [illegible] tubules; they secrete a lytic subst[illegible]el in the host tissue through whic[illegible]mbryo of certain tapeworms is also provided with glands, the secretions of which [illegible]

cystogenous glands in the hypodermis. The fluid "sets" to form a more or less resistant membrane around the larva. Such glands atrophy when their temporary function has been served. Some adult flukes also have clusters of glands in the region of the mouth but their use is not well understood. In the case of the hookworm there are glands present in the region of the buccal opening which possibly have an anti-coagulating, as well as histolytic action, so that the worm, when once attached to the intestinal mucosa of the host by its buccal armature, may have a continuous supply of uncoagulated blood, as well as predigested mucosa cells, for its food.

The by-products or metabolites of the endo-parasitic helminths may be grouped into two classes: (1) The ordinary katabolic wastes produced by the worm, which may or may not be harmful to the host, and (2) specially elaborated secretions, which have a deleterious effect on the host. If the worm lives in the digestive tract, its waste products ordinarily pass out with the excreta and, unless there is an overwhelming infection, little harm to the host results. Certain worms, however, whether free, firmly attached to the intestinal wall, or resident in the more intimate tissues of the body, discharge secretory products which are absorbed into the tissues and which are believed to produce very definite local, or systemic reactions. Thus, hookworm disease and broad fish tapeworm infection are occasionally associated with an anemia which resembles a pernicious type, although the usual blood picture in these infections is that of a hypochromic, microcytic erythropenia. The blood flukes and *Trichinella* larvæ cause a profound eosinophilic reaction. *Ascaris*, *Trichocephalus* and *Hymenolepis* give rise to nervous symptoms, particularly among small children. These and other

worms at times give rise to hypersensitization reactions and to severe hematuria.

All of the structural adaptations of helminths for protection against the digestive and abrasive processes constantly at work in the intestinal lumen of the host, as well as those assisting the worm to secure a better attachment to host tissues, are to be reckoned with by the physician in estimating the seriousness of a particular infection and even to a greater degree in therapeutic procedure. Since the integument of most of the adult worms has been developed to resist action of the digestive juices of the host's body, it also resists the action of many of the drugs which are in common use by the clinician. Whether the worm lies free in the intestinal lumen, as *Ascaris* normally does, or attached to the intestinal wall, as the hookworm, tapeworm, and *Fasciolopsis*, or imbedded in the intestinal mucosa, as *Strongyloides*, *Trichinella*, *Metagonimus* and *Heterophyes*, or has its head deeply inserted into the intestinal wall, as *Trichocephalus*, a drug to be potent must be (1) either narcotizing or lethal to the worm, and (2) at the same time, must be capable of reaching the place where the head of the worm is attached, so that it will be absorbed into the inner soft tissues of the worm, killing the tissue, or at least causing the muscles to relax and the normal activities of the worm to be inhibited. [illegible] ments it is valueless as an anthelmintic [illegible] also to the blood flukes and the "live [illegible] namely, that the drug, in order that it may be effective, must actually reach the focus of infection in narcotizing or lethal doses.

The most conspicuous increase in organs or tissues of the helminths as a group is that of the reproductive system. Both the Platyhelminthes and the Nematoda have a large part of their body-mass occupied by these organs and their products. The adult flatworms are, with few exceptions, hermaphroditic; the roundworms are almost entirely diecious. In both groups the volume of reproductive products is enormous for the mass of the worm. The rapidity with which these products are manufactured is equally astounding. The description of important types of reproductive organs will be found under the sections in the text dealing with the respective groups of helminths.

The adult flukes and tapeworms have particularly complex reproductive organs, directed towards one end, *i. e.*, the production of as many eggs as possible with the fewest opportunities for mishap to these reproductive products. To this end, in both groups, cross-fertilization, which was formerly the rule and is still a possibility, has been mostly superseded by self-fertilization. In the tapeworms, instead of a single body unit there are multiple "segments" or proglottids, each one sexually complete in itself. Thus, a single worm may produce fertilized eggs numbering into the tens of thousands daily. While all of the parasitic roundworms of man, with the possible exception of *Strongyloides*, require a male attendant upon the female for the production of viable eggs, the life cycles of the members of this group are, as a rule, somewhat less complicated than those of the flatworms, so that to them this requirement is not a serious handicap. In certain cases, however, infection with a single sex produces complications for the diagnostician. The unfertilized eggs of *Ascaris*, frequently indica-

tive of infection with females only, are very different in appearance from the fertilized ones. Infections with only male worms of these and other species cannot be diagnosed by the recovery of eggs in the feces, so that diagnosis must be made in less direct ways such as objective and subjective symptoms, followed by therapeutic tests. While a single male hookworm has no clinical significance (and it is highly improbable that any considerable number of males would be present in an infection without at least one female being in the group), infection with a single male *Ascaris* frequently produces sufficient digestive and nervous symptoms to justify therapeutic procedure.

Although the majority of parasitic roundworms have no reproductive stage outside of the host in which the adult worms reside, *Strongyloides* frequently has at least one free-living generation alternating with the parasitic one. The majority of the tapeworms likewise have no reproductive cycle outside of their final host; however, the larvæ of *Multiceps, Echinococcus* and, at times, *Diphyllobothrium* are exceptions to this rule. These latter species are all of special clinical importance, since the larval stage of each of these species is known to parasitize man.

In all of the trematode parasites of higher animals, there are always two reproductive generations outside the definitive host. These occur in the mollusc. Thus, in *Schistosoma japonicum* infections, where each female worm lays several hundred eggs per day, it is probable that the larva (*i. e.*, the miracidium) from each viable egg, after hatching and penetrating the tissues of the appropriate snail, gives rise by a two-generation propagation to 10,000 or more progeny, capable of infecting the human host. Unlike bacteria, however, the majority of the adult helminths, once arrived in their final host, do not multiply within that host, although in certain helminthic infections the eggs, when laid and extruded into the tissues, are undoubtedly more pathogenic than the worms themselves.

Two systems of organs, the nervous system and the excretory system, the former in all parasitic helminths and the latter particularly in the trematodes, have been little altered in the adaptation of the organism to a parasitic existence. They are, therefore, of little significance to the clinician, but to the medical zoölogist they are very useful in showing the relationship of species, genera and families one to the other. The arrangement of the excretory system, which has been found to be identical in the cercarial larva of the three human schistosome species, is an admirable illustration of this fact.

Viewing the group of parasitic helminths as a whole with respect to the successive stages of adaptation which they have undergone and are undergoing, one is able to appreciate how vast and how profound have been the alterations from a free-living existence, and how dependent the parasite is upon the host, when once it has become so adapted.

Because parasitism is so wasteful in the production of reproductive cells that never reach the next host, particularly where two or more hosts are involved in the same life history, the reader may rightly wonder that the life cycles are completed at all. Yet under suitable conditions the parasite multiplies so enormously and produces such ravages in its hosts that eradication or control of the infection can only be effected by the most

energetic measures, based on a thorough understanding of the epidemiology of the infection. From a preventive standpoint it is, therefore, essential that the physician appreciate the epidemiology and biology, as well as the pathology, symptomatology, diagnosis and treatment of helminthic infections. Likewise, from a standpoint of anthelmintic medication, it is necessary that the physician acquaint himself thoroughly with the habits of the parasite, as well as the drug of choice, its dosage and its contraindications for a particular infection or group of infections, in order that he may manage the case satisfactorily.

GLOSSARY OF ZOOLOGICAL AND MEDICAL TERMS

Abscess.—An inflammatory process, consisting of a collection of infiltrated polymorphonuclear cells around localized necrotic tissue, in a liquid or semi-liquid

"sucker."

Agglutination.—Clumping or agglomeration of microorganisms or their parts resulting from introduction of serum or other electrolyte containing specific antibody.

Allergenic.—Inducing allergy

Allergy.—Exaggerated sensitiveness on the part of certain individuals to specific substances in amounts producing no appreciable reaction in the majority of individuals of the same species. (See *anaphylaxis*.)

Amphid.—One of a pair of chemo-receptors situated at the anterior end of nematodes.

Anaphylaxis.—Hypersensitization to a protein or other undenaturized substance introduced into living tissues following previous sensitization to such substance. (See *allergy.*)

Anemia.—A deficiency in the quality or quantity of the red blood cells.

number.

Microcytic.—Decreased size of red blood cells usually associated with a decrease in their number.

Normocytic.—Reduction in number of red blood cells without change in their size

Antibody.—Specific substance produced by living tissue as a reaction to the introduction of a natural foreign protein or other undenaturized material.

Antigen.—Any substance which, on introduction into the tissues, causes production of antibody

Asymptomatic. Without subjective evidence of disease

Asyndromic.—Lacking symptoms which are usually associated in an infection

Autoinfection. Reinfection without exposure from the environment, self-infection

Bursa (copulatrix).—Umbrella-like expansion of the caudal end of the male in certain groups of nematodes (*i. e.*, bursate nematodes).

Capsule.—A membrane or wall laid down by host's cells around living or inert foreign bodies, being a protective reaction of the host, likewise a membranous or fibrous covering of an organ, as the liver, spleen, kidney or adrenal gland

Carrier.—A host which harbors a particular pathogen without manifestations of disease.

Celomyarial. Muscle structure in nematodes, in which the muscle fibers are not

only next to the subcuticula but "also extend varying distances up the side of the muscle cell and partially enclose the sarcoplasm" (Chitwood, 1934, 1937).

Cercaria.—The larva (usually possessing a tail) which escapes from a sporocyst or redia generation of a trematode within the molluscan host, and constitutes the transfer stage to the next host.

Cercariæum.—Cercaria with a tail underdeveloped or lacking.

Cercomer.—In a tapeworm embryo, the caudal vestige of the oncosphere, containing the six hooklets.

Chronic Stage.—A post-acute period in which the symptoms are less severe as a result of tolerance or repair of damage.

Chylocele.—A condition in the tunica vaginalis of the testis due to milky effusion from the lymphatic vessels, as in Bancrofts' filariasis.

Chyluria.—A milky or cloudy condition of the urine resulting from discharge of lymph into the urinary bladder.

Cirrhosis.—Diseased state (of the liver) resulting from thickening, fibrosis and shrinking of the supporting tissue, usually causing decrease in size of the organ and a nodular surface.

Cirrus.—Retractile muscular organ at the outer end of the male reproductive system of species of Platyhelminthes.

Cœnurus.—Larval cystic stage of the tapeworm *Multiceps*, containing an inner germinal layer producing multiple scolices within a single cavity. (See *cysticercus* and *hydatid*.)

Commensal.—An organism which lives at the expense of another without causing damage to the latter.

Complement fixation.—On union of antigen and antibody, active complement in the medium causes hemolysis of sensitized red blood cells.

Contaminator.—An organism or other object which occurs fortuitously or accidentally.

Control.—Effective reduction in exposure to a disease, causing a decrease in incidence of the disease.

Coprophage.—An organism which feeds on feces (or dung).

Coprozoite.—An animal which feeds on feces.

Coracidium.—In tapeworms, the oncosphere enclosed in its embryophore *after* hatching from the egg shell.

Cotylocercous (cercaria).—Cercaria with a short, cup-like tail used as an organ of adhesion or attachment.

Cure.—Successful treatment.

Biological.—Eradication of the etiological agent.

Clinical.—Treatment which provides freedom from symptoms and thus improvement in the patient's condition.

Cuticula.—In helminths, the covering layer secreted from the epidermis, hypodermis or subcuticular layer.

Cyst.—An organism together with the enveloping membrane or wall secreted by that organism; therefore the encysted organism.

Cysticercoid (larva).—Larva of tapeworms in which the scolex is invaginated into a greatly reduced cystic cavity almost devoid of fluid.

Cysticercus (larva).—Larva of tapeworms in which the scolex is invaginated into a bladder filled with fluid.

Cystophorous (cercaria).—Cercaria with a bulbous chamber at the base of the tail, into which the body of the cercaria is retracted.

Defense mechanism.—The humoral and cellular reaction to invasion.

Deirid.—One of a pair of tactile papillæ in the cervical region of certain nematodes.

Diagnosis.—Discovery of the nature and etiology of disease.

Clinical.—Diagnosis based on manifestations of disease.

Diecious.—Female and male reproductive organs in different individuals

Digenetic.—Three or more generations (literally "two") required for completion of one life cycle, as in digenetic trematodes.

Dysentery.—Passage of frequent stools usually containing blood, mucus and cellular detritus, resulting from an inflamed or ulcerated condition of the intestine. (See *diarrhea.*)

Ectoparasitic.—Living upon or in the superficial tissues of another organism

Ectopic.—Outside the normal location, as the position of a parasite which has reached an atypical site.

Egg.—The completed sex product following fertilization (if this occurs) of the female reproductive cell or ovum, the addition of yolk and other nutritive materials, the embryonic membrane and other shell layers

Ejaculatory duct.—The muscular terminus of the male genitalia of nematodes, opening into the cloaca.

Embryo.—The stage in development following cleavage of the egg up to, but not including, the first larval stage

Embryophore.—In tapeworms, the envelope immediately around the oncosphere and derived from it

Endemic.—Continued prevalence of a disease in a human community. (See *epidemic.*)

Endoparasitic.—Living within another organism, including the digestive tract of the latter

Enzoötic.—Continued prevalence of a disease in animals. (See *epizoötic*.)

Eosinophil.—Polymorphonuclear leukocyte, with granules having an affinity for eosin dye

Eosinophilia.—Increase of eosinophils in the circulating blood in excess of 4 per cent

Epidemic.—A sharp increase or an outbreak of a disease in a community. (See also *endemic*.)

Epidemiology.—The sum of knowledge concerning the propagation of diseases

Epidermis.—The outermost layer of tissue of a metazoan organism

Epithelioid cell.—Cell with abundant protoplasm, phagocytic in nature, present in foreign-body type of reaction, believed to originate from histiocytes

Epizootic.—A sharp increase or an outbreak of a disease in animals

Eradication.—Complete elimination of an etiological agent in an individual, a group of persons or a community

Exposure.—Opportunity or circumstances which allow entrance of parasites into the body of the host.

Fibrocyte.—Elongated cells derived from connective-tissue cells, the fibroblasts, functioning in the production of fibrous tissue

Fibrosis.—Diseased state of an organ or tissues due to infiltration of fibrocytes, with subsequent deposition of fibrous tissue, in the process of repair

Filariform (larva).—A post-feeding-stage nematode larva characterized by its delicate, elongate structure and its slim, capillary esophagus

Flame cell. See *solenocyte*

Furcocercous (cercaria).—Fork-tailed, as the cercaria of schistosome, strigeid, clinostomatid and gasterostome trematodes.

Genital atrium.—In Platyhelminthes, the antechamber to the genital tubules

Giant cell.—Large multinucleate cell of the reticulo-endothelial system, frequently present in foreign-body type of reaction and leading to production of granulomas

Gonotyl.—Genital sucker, retractile and associated with, or incorporated into, the ventral sucker, in certain species of Heterophyidæ (trematodes).

Granuloma.—A tumor made up of granulating tissue, at times produced around a number of pseudo-tubercles.

Gravid.—Filled with eggs, as a gravid pinworm or gravid proglottid of a tapeworm.

Gubernaculum.—A small, sclerotinized, accessory structure in male nematodes, associated with the spicules.

Gymnocephalous (cercaria).—Literally, "naked headed"; cercariae without ornamentation of body or tail, as the cercaria of *Fasciola hepatica.*

Gynecophoral canal.—In certain male schistosomes, the incurved portion of the body extending from the ventral sucker to the caudal extremity, for carrying the female during insemination and oviposition.

Haptor.—Organ of attachment; an acetabulum, as the pre-oral, oral, or ventral sucker of trematodes

Hematemesis.—Blood in the vomitus.

Hematuria.—Blood in the urine.

Hemoptysis.—Discharge of blood from the respiratory tract.

Hermaphroditic.—Containing both male and female reproductive organs; monecious.

Heterogonic.—Development in which both females and males are present in a colony.

Hexacanth embryo.—"Six-hooked" embryo, the mature embryo within the egg of many tapeworms, including all species which parasitize man.

Histiocyte.—Large phagocytic cells of the reticulo-endothelial system.

Fixed histiocyte.—Attached to wall of sinusoids, as Kupffer cells of the liver.

Wandering cell.—Histiocytes which migrate through tissues and body fluids.

Hologonic.—Development in which only one sex (usually the female) is present in a colony.

Holomyarial.—Muscle arrangement in nematodes, in which the cells are small, numerous and closely associated so as to appear like a single band. (See *meromyarial* and *polymyarial.*)

Host.—An organism which harbors and nourishes another.

Alternate host.—One which alternates with another in the life cycle of a parasite. Mosquitoes and man are alternate hosts of Bancroft's filaria.

Definitive host.—One in which the terminal (frequently sexual) stage of the parasite occurs. Man is the definitive host of Bancroft's filaria.

Intermediate host.—One which alternates with the definitive host and frequently harbors the larval stage of the parasite. Man is an intermediate host of *Taenia solium* as well as the definitive host.

Reservoir host.—One in which the infection usually resides; also one which harbors the parasite when man is not infected. Ruminants are reservoir hosts of most species of *Trichostrongylus* (nematodes).

Hydatid cyst.—Larval cystic stage of the tapeworm *Echinococcus,* containing an [illegible] ito the cystic [illegible] community.

Hyperinfection.—Internal autoinfection, as in strongyloidiasis, oxyuriasis or hymenolepiasis nana. (See *autoinfection.*)

Hypodermis.—In helminths, the layer of tissue immediately below the epidermis [illegible] sure or vaccination.

Passive.—Immunity resulting from introduction of immune bodies developed in another host.

Incubation Period.—*Biological.*—From the time of invasion of the host until maturity of the parasite, the prepatent period.

Clinical.—From the time of exposure until the appearance of symptoms.

Infectible.—Capable of, or susceptible to, infection

Infection.—Existence of parasitic organisms *within* the body of the host; *endoparasitism.*

Infectious.—Containing the property of producing infection.

Infective.—Stage of a parasite capable of producing infection.

Infestation —Existence of parasitic organisms on the outside of the body of the host, or in the superficial tissues; *ecto-parasitism.*

Inoculation.—Active or passive introduction of parasites into the body of a host, without necessarily denoting a "take" or infection; also introduction of an inoculum into a culture medium

Intradermal reaction —Development of an inflammatory or edematous wheal in the skin, following introduction of antigen homologous to antibody produced in the tissues.

Larva.—The post-embryonic stage, in which internal organs are developing or are developed and are at least partially functioning.

Laurer's canal —In trematodes, a tubule leading from the dorsal surface to the region of the ootype and seminal receptacle, it may be patent, vestigial or lacking.

Leukocytosis —Increase in number of the white blood cells

Leukopenia —Decrease in number of white blood cells below average.

Longitudinal "lines."—In nematodes, four cords, one median dorsal, one median ventral and two median lateral, extending from the anterior to the posterior [illegible]

Ly[illegible] small amount of cytoplasm, arising from lymphoid tissue.

Lymphocytosis —Increase in number of the lymphocytes

Lysis —Digestion of cells or tissues by enzymatic action.

Macrophage —A large phagocytic cell of the body.

Mature (proglottid) —Containing fully developed reproductive organs of tapeworms

Mehlis' glands —In Platyhelminthes, the glands surrounding the oötype

Meromyarial —Muscle arrangement in nematodes, in which there are only a few, frequently only two, flat muscle cells in each quadrant of a cross section of the worm. (See *holomyarial* and *polymyarial*)

Metabolite —Any by-product of a living organism.

Metacercaria —The stage of trematodes succeeding the cercaria, following loss of the tail This stage may actively invade the definitive host (blood flukes) or may become encysted and await passive transfer to that host. (See *schistosomulum*)

Metagenesis.—Alternation of sexual and asexual reproduction

Metraterm —The muscular, terminal portion of the uterus in Platyhelminthes.

Microcercous (cercaria) —Cercaria with a short, stumpy tail, as the cercaria of *Paragonimus westermani*

Microfilaria. The uncoiled embryo of a filaria, which either escapes from the egg shell (*i e*, is "unsheathed") or causes stretching of the shell into an elongated sac accommodated to the uncoiled embryo (*i. e*, is "sheathed")

Miracidium The larva hatched from the egg of trematodes

Monecious – Containing both female and male reproductive organs in the same organism or reproductive unit; hermaphroditic.

Monocyte A large leukocyte with slightly curved nucleus and appreciable cytoplasm

Monocytosis Increase in number of circulating monocytes in the blood.

Monogenetic A single generation constituting a complete life cycle, as in monogenetic trematodes

Neutropenia.—Decrease in number of neutrophils below average.

Neutrophil.—Polymorphonuclear leukocyte, with granules having a neutral staining reaction.

Normoblast.—Immature red blood corpuscle which still has a nucleus.

Nosogeography.—Knowledge concerning the geographical distribution of diseases.

Oncosphere.—The stage which hatches from the egg shell and later escapes from the embryophore of tapeworms; in human tapeworm infections it is 6-hooked (*i. e.*, a hexacanth embryo).

Ootype.—The chamber in the reproductive system of Platyhelminthes where typically the several components of the eggs are assembled.

Ovejector.—A muscular organ in some female nematodes which forces eggs from the uterus into the vagina.

Oviparous.—Egg-laying. (See *viviparous.*)

Ovum.—The naked, mature female cell preceding the addition of an embryonic membrane and outer shell layers.

Pandemic.—Wide-spread epidemic.

Parasite.—An organism which lives at the expense of another organism.

Facultative.—One which may employ either a free-living or a parasitic mode of life.

Obligatory.—One which necessarily lives a parasitic existence.

Parenchyma.—In Platyhelminthes, the loose, usually undifferentiated tissue which forms a matrix in which the viscera are embedded.

Parthenogenesis.—Production of progeny from the ovum without fertilization.

Patent.—Open or apparent, as indicated by unmistakable signs, like eggs in the feces or microfilariae in circulating blood.

Pathogen.—A parasite causing injury to a host. (See *commensal* and *parasite.*)

Pathogenesis.—Development of disease-producing processes in an organism.

Pathognomonic.—Characteristic of a disease process.

Pathology.—The sum of information concerning disease-producing processes.

Phagedenic.—A sloughing, spreading, chronic, ulcerated condition.

Phagocyte.—Scavenger cell.

Phasmid.—One of a pair of caudal chemo-receptors in certain nematodes (*i. e.*, the Phasmidia).

Platymyarial.—Muscle structure in nematodes, in which the muscle cells all lie next to the subcuticula and their sarcoplasm is uncovered on three sides next to the body cavity (Chitwood, 1934, 1937).

Plerocercus (larva).—A tapeworm larva in which the scolex is embedded in a greatly enlarged tail, *i. e.*, a sparganum, *as in Diphyllobothrium latum.*

Pleurolophocercous (cercaria).—A small cercaria, with pigmented eyespots, an anteriorly directed, protrusile oral sucker, numerous salivary glands, and a long, powerful tail provided with a pair of fin folds.

Pneumonitis.—Localized inflammation of the lungs; atypical pneumonia.

Polyadenous (cercaria).—Cercaria with a stylet and paired groups of penetration glands. Example: *Cercaria polyadena* Cort, 1914.

Polymorphonuclear leukocyte.—White cells with nuclei which are segmented when mature, typically containing granules. They are classed as neutrophils, eosinophils and basophils.

Polymyarial.—Muscle arrangement in nematodes, in which there are many muscle cells in each quadrant of a cross section of the worm. (See *holomyarial, meromyarial.*)

Precipitation reaction.—Non-specific, particulate precipitate, occurring from introduction of distilled water into blood plasma and due to excess globulin formation in certain diseases.

Precipitin test.—Demonstration by fine precipitation of specific antibody in blood plasma on introduction of homologous antigen.

Predacious.—Having the characteristics of a predator.

Predator.—An animal which kills or renders its victim insensible in order to consume it in whole or in part.

Prepatent period —The biological incubation period.

Proboscis.—In Acanthocephala and in the dog tapeworm (*Dipylidium caninum*), anterior protrusile organ, typically studded with hooklets

Procercoid (*larva*).—The first larval stage of pseudophyllidean tapeworms, which develops from the oncosphere, it contains a body proper and caudal vestige of the oncosphere, the cercomer. (See *cermoner.*)

Proglottid —One complete unit of a tapeworm, commonly called a "segment"

Prophylaxis.—Prevention.

Pseudo-abscess—A collection of infiltrated host's cells, primarily of the reticulo-endothelial type, around a living or inert foreign body, as around infiltrated helminth's eggs. (See *abscess.*)

Pseudocele.—Body cavity of nematodes, not lined with mesothelium, same as schizocele

Pseudo-parasite —An object (living or dead) which may be confused with a parasite, a spurious parasite

Pseudo-tubercle.—A foreign-body reaction resembling a tubercle but not provoked by tubercle bacilli (See *tubercle.*)

Refractory —Not readily infectible, likewise not amenable to therapy.

Reticulocyte —Young red blood corpuscle, more mature than a normoblast, but retaining a reticulum which is revealed by intravital staining

Retrofection.—In oxyuriasis, a variety of autoinfection in which larvæ hatch from [illegible] ...us is [illegible], the body

Rostellum The somewhat protruberant apical portion of the scolex of certain tapeworms, fr[illegible] *T*[illegible] *solium.*

Saprophage [illegible]

Saprozoite [illegible]

Schistosomulum —Immature stage of schistosomes or blood flukes, from the time of entry into the definitive host until the worm reaches sexual maturity. (See *metacercaria*)

Schizocele.—Body cavity in nematodes, not lined with mesothelium, same as pseudocele

Scolex —Attachment end of a tapeworm, commonly referred to as the "head"

Seminal receptacle (*receptaculum seminis*) —The storage reservoir for spermatozoa in the female.

Seminal vesicle (*vesicula seminalis*).—The storage reservoir for spermatozoa in the male

Sensitization - Process or state of sensitiveness or hypersusceptibility to specific substances in contact with body tissues.

Sign. Objective evidence of disease.

Solenocyte.—Literally, "canal cell." In Platyhelminthes, the cell with a tuft of cilia at the head of each capillary in the excretory system; commonly called "flame cell"

Sparganum. The second larval stage of pseudophyllidean tapeworms, characterized by its elongated shape and lack of a cystic cavity; it is a plerocercus larva

Spicules (*copulatory*) —Two, or at times only one, bristle-like, lanceolate or hastate, sclerotinized structures in the outer genital chamber of male nematodes, introduced into the vulva or vagina of the female at times of insemination

Sporadic Occasional occurrence, as of a disease

Strobila.—A complete tapeworm, consisting of scolex, "neck," immature, mature and usually gravid proglottids.
Strobilization.—Asexual production of a series of sexual reproductive units, as in a tapeworm.
Superinfection.—New infection superimposed on an existing one of the same kind.
Symbiont.—One of two organisms which live together to the advantage of both.
Symbiosis.—State of two organisms living together for mutual advantage.
Symptom.—Any evidence, subjective or objective, of disease in a patient.
Syndrome.—A set of associated symptoms.
Syngamy.—Permanent union of both female and male reproductive units; at times the male element is greatly reduced and is parasitic in the female.
Tetrathyridium.—In the tapeworm genus *Mesocestoides*, the second larval stage in which the scolex with its four suckers is invaginated into the anterior end of a plerocercus type of body. (See *plerocercus.*)
Therapy.—Treatment or medication.
[illegible]

Toxin.—A poisonous substance in the secretions or excretions of a parasite
Trauma.—Injury produced by mechanical processes, by digestion, erosion, toxins or indirectly by inflammation.
Trichocercous (cercaria).—Cercaria having a tail provided with conspicuous spines or bristles
Uterus.—The tubule containing the fully formed eggs.
Vagina.—An outer chamber of the female genitalia in nematodes; also the tubule leading from the genital atrium to the oötype in Cestoidea. (See *vulva.*)
Varix—An enlarged, tortuous vein, artery or lymphatic vessel.
Vas deferens.—The common male duct arising from one or more vasa efferentia and leading into the seminal vesicle.
Vas efferens.—The male duct conveying spermatozoa from the testis to the vas deferens.
Vector.—A transmitter of parasites
  Biological vector.—A host essential to development and transmission of a parasite
  Mechanical vector.—A non-essential disseminator of parasites
Vermicide—Therapeutic agent which produces death of a helminth.
Vermifuge.—Therapeutic agent producing evacuation of a helminth without necessarily causing its death.
Vitellaria (vitelline glands).—The glands in Platyhelminthes which produce yolk material and probably also the shell of the egg.
Vitelline membrane.—The innermost layer in the shell of fertilized eggs of helminths.
Viviparous—Discharging living young. (See *oviparous.*)
Vulva—The outermost, unpaired chamber of the female genitalia in nematodes.
Worm burden.—The number of worms present in the host.
Xiphidiocercaria.—Cercaria with a stylet, median dorsal in position in the oral sucker, having associated penetration glands with duct openings on either side of the stylet.

CHAPTER II

THE FOUNDATIONS OF HELMINTHOLOGY

THE ANTIQUITY OF HUMAN HELMINTH PARASITES

ALTHOUGH parasitism in the Animal Kingdom has undoubtedly been a relatively recent event when compared with the main lines of development of free-living groups of organisms, it was unquestionably well established millions of years before the dawn of human history; and, while the distribution of various species of parasites may have been altered within historic times by the migration of the races, it is reasonably certain that all of the common species of human parasites are far older than the human race itself. The evidence for such belief is necessarily *a priori* but nevertheless convincing. Some of the present-day parasites of man are lineal descendants of those which adapted themselves to man's simian ancestors, while others are common in the animals which man domesticated. Certain infections which are apparently non-pathogenic for other animals, cause severe symptoms in man, thus giving evidence of a shorter period for adaptation in the human species. Furthermore, many of the parasitic forms which now require two or more hosts, including man, in which to complete their life cycles, may have originally only utilized one, the present larval host, or, in the filaria worms, possibly the present definitive host, with the developmental larvae in the Arthropod host as free-living stages. Finally, physiological differences among parasitic species in man and other mammals, where morphological structures appear to be identical, indicate that the parasite has become established in man sufficiently long to have acquired a relatively fixed adaptation.

Referring particularly to the human helminth parasites, certain species, which require a period of development outside of the human body, probably adapted themselves slowly from a free-living to a parasitic existence. This latter point is well illustrated in the instance of several nematode parasites infecting man. *Strongyloides*, which can probably live indefinitely outside the body, is undoubtedly a recent human parasite. The hookworm, which exists for the period of its larval development as a free-living organism, presumably has a longer history as a parasitic organism, while *Ascaris*, and to an even greater extent, *Trichocephalus* and *Enterobius*, show evidence of long-continued existence as essentially parasitic species. The helminth *parasites of the blood and lymph channels have undergone more profound* adaptations, particularly of a physiological character, than those of the digestive tract or its outpocketings, suggesting that the former are possibly far the older.

Thus, essentially all of the helminth parasites of man of the present time must have been human infections a hundred thousand years ago, while other infections now found almost exclusively in domestic mammals but potentially parasites of man, must have also been man's burden in earlier times. The Glacial Age hunter of wild oxen and wild boars became infected with tapeworms, *Ascaris* and *Trichinella*. The primitive fisherman

acquired, with his consumption of raw fresh-water fish, fish tapeworm (*Diphyllobothrium*) and certain liver-fluke infections (opisthorchiasis, clonorchiasis). The herdsman, mingling with his sheep and his dogs, was exposed to hydatid disease. As he drank from an oasis pool, where a previous traveller had bathed, he subjected himself to *Dracunculus* infection. Insects stung his unprotected body and in so doing conveyed filarial infections to him. As he began to settle down and till the soil, he came more and more in contact with others of his own species and race, so that unhygienic conditions developed from the accumulation of infected human excreta, with the result that hookworm disease and infections with *Strongyloides*, *Ascaris* and *Trichocephalus* became endemic. In the Nile and in the Yangtze valleys fishermen and farmers wading about in the irrigation canals acquired schistosomiasis. The rat conveyed *Hymenolepis* infection and the dog flea, *Dipylidium* infection. So at the dawn of history foyers of helminthic infection were distributed throughout the entire habitable world.

KNOWLEDGE OF HELMINTHIC DISEASES BY ANCIENT PEOPLES

The annals of the Accadian peoples refer to *Ascaris* and tapeworm. The Eber's Papyrus (16th century B.C.) is the oldest record in which a helminth is regarded as a pathogenic organism, the diseases "A A A" and "U H A" being attributed to a worm ("Heltu"). Although it is impossible to say whether the worm referred to is an *Ascaris*, a hookworm, a tapeworm or some other helminth, it is interesting that symptoms were attributed to the presence of this "bowel worm" and that a remedy, extracted from the bark of the pomegranate tree, *Punica granatum*, was prescribed for its expulsion The use of quisqualis seeds and betel nut by the Chinese as vermifuges also dates back into early historical records. Egyptian mummies have furnished evidence of the existence of *Schistosoma hæmatobium*, the causative organism of vesical schistosomiasis, in the Nile delta during the 13th century B.C. (i e., calcified eggs of this worm found in the kidneys of two mummies of the 20th dynasty, identified by Ruffer, 1910).

The Hebrews were instructed in the laws of sanitation and hygiene by Moses, who had secured his learning from the Egyptian priests. The "fiery serpent" in the wilderness of Sinai was probably the Medina or Guinea worm, *Dracunculus medinensis*, and the likeness which Moses made by winding the "serpent" around a rod (Numbers 21 5–9) is believed by some medical historians to have served as an example for the people in extracting the worm from their tissues by winding it around a stick, the simple method employed by Arabs and Africans in infected areas today Moses likewise separated the animals into "clean" and "unclean" on the basis of those free from, or infected with, visible parasites. This was particularly true of goats and kids, first offered for sacrifice and later eaten by the priests Goats in Syria today are heavily infected with *Fasciola hepatica*, and the people eating the infected raw livers acquire "halzoun" (*i. e*, "suffocation") or pharyngeal fascioliasis All scavenger beasts and birds were prohibited from use as food, including hogs and camels, birds of prey, reptiles, snails, etc, because their flesh was infected with parasites (Lev. 11). Likewise all animals not on the prohibited list, whose flesh was found infected, were required to be burned (1490–1450 B.C.). Furthermore, Moses advised the people to beware of "infected water," which, no doubt, at that time, as today, contained *Cyclops*, infected with the larvæ of the Medina worm (*Dracunculus medinensis*), as well as the free-swimming cercariæ of *Schistosoma hæmatobium*. Later the Hebrews were instructed in the method of drinking water from their hands rather than lapping it up directly from a stream,

possibly so as to avoid the ingestion of blood-sucking leeches (Gideon's army, *vide* Judges 7:5-7).

Aristotle mentions tapeworms. Echinococcus disease was diagnosed by the Greek physician Hippocrates, who described an operation for removal of the hydatid cyst. This parasite was also known to Aretæus and to Galen.

The most ancient medical record in the Christian Era, of interest to the helminthologist, is that of Avicenna, a Persian physician, who was born in 981 A.D. and died in 1037 A.D. He described four kinds of worms: (1) Long worms, apparently [illegible]

proglottids of *Tænia saginata*, acquired from eating raw beef, a custom common among butchers in the slaughter houses of Cairo today, often found in the small intestine, [illegible] of the anus, causing a [illegible] them a very potent an[illegible] ms, probably *Enterobius vermicularis*, common in the cecum and colon, often migrating out of the anus, causing little harm, but producing discomfort in the form of itching around the buttocks; for them enemata with salt water were recommended; (4) roundworms, probably the common *Ascaris lumbricoides* found in the small intestine, more frequent in boyhood and early maturity than in old age, producing "malignant" [illegible]

The early Persian physicians also correlated elephantiasis with the presence of a filaria worm

THE BEGINNING AND DEVELOPMENT OF MODERN HELMINTHOLOGY

[illegible]

Swammerdam (1752), Rosenhof (1758), O. F. Müller (1773), Goeze (1800) and Zeder (1790, 1800) are all associated with observations on trematode species, principally of a descriptive nature. At first these worms were referred to as "sucking worms" and were confused with the leeches. In 1808 Rudolphi gave the group the name "Trematoda," from τρηματώδα or "body pierced with holes." For the next [illegible]

fluke, *Fasciolopsis buski*, and Bilharz (1851), the human blood fluke, *Schistosoma hæmatobium*, and the small intestinal fluke, *Heterophyes heterophyes*. There followed the finding of *Clonorchis sinensis* by McConnell in 1874, of *Paragonimus* by Kerbert [illegible]

come within the last few decades. First and most important was that of *Schistosoma japonicum*, the causative organism of Oriental schistosomiasis, which had been recognized by the Japanese as a disease entity since 1847. Starting with the classical work of Fujinami (1909), who showed that water from irrigation ditches in endemic areas was the source of infection, various Japanese investigators, including Miya-

gawa (1912) and Miyairi and Suzuki (1913) first traced the route of invasion of the parasite through the mammalian body, from the skin to the mesenteric veins, and later demonstrated the rôle of the amphibious snail, *Oncomelania* (*Katayama*) *nosophora*, as intermediate host in the infection. Later Faust and Meleney (1924) found that the related mollusc, *Oncomelania hupensis*, as well as *O. nosophora*, were responsible for the infection in China, where approximately 100,000,000 persons were yearly subject to exposure. In 1915 Leiper worked out the life cycles of *Schistosoma hæmatobium* and *S. mansoni* in Egypt, showing that these blood flukes also required a snail for [illegible] that they were separate species. [illegible] –1919), Ando, (1917), Yoshida [illegible] 919) on *Paragonimus*, in which these investigators found not only molluscs but fresh-water crabs and crayfish involved; the investigations of Yokogawa and others on *Metagonimus*, in which both molluscs and fresh-water fishes were incriminated; the work of Nakagawa (1921) and Barlow (1925) on *Fasciolopsis buski*, demonstrating that the life cycle of this fluke followed closely that of *Fasciola hepatica* and that water plants were the agents of human infection; and, finally, the extensive studies of Kobayashi (1910–1917), Muto (1918), Nagano (1925–1926), Faust and Khaw (1924–1927) and Hsu (1936–1939) on *Clonorchis sinensis*, demonstrating that this infection required as a first intermediate host a bithynoid snail and later, as second intermediate hosts, fresh-water fishes, consumption of which in the raw state brought about the infection; and that practically all of the cyprinoid fishes in the Sino-Japanese areas were naturally infected with the encysted larvæ of this fluke. The convincing investigations of Vogel (1934) on the developmental cycle of *Opisthorchis felineus* may also be regarded as one of the fundamental life-cycle studies on human trematode parasites. The recent studies of Cort and his associates (1942–1948) on the germ cell cycle in trematodes have added renewed interest in this fundamental phase of biology.

As has been stated previously, tapeworms were known to the Greeks. In 1592 *Tænia* was distinguished from *Diphyllobothrium* (*Dibothriocephalus*). Redi (1687–1695) recognized the larval stage of *Tænia*, the *cysticercus*, as an animal form. Not until 1851, however, did Kuchenmeister prove by feeding experiments that these bladder worms represented the alternate or immature phase of the life cycle of the tapeworm and that, as a rule, they required a different host from that of the adult worm. The life history of the pork tapeworm, *Tænia solium*, was first worked out by Kuchenmeister (1855) and Leuckart (1856). The investigations of Leuckart (1861), Mosler (1863), Oliver (1869) and Perroncito (1876–1877) proved that the beef tapeworm, *Tænia saginata*, required a similar alternation of larval and adult hosts. Von Siebold (1852), Kuchenmeister (1861), Leuckart (1862) and Naunyn (1863) elucidated the life history of the hydatid worm, *Echinococcus granulosus*. The dwarf tapeworm of man, *Hymenolepsis nana*, first discovered by Bilharz in Cairo (1851), was believed by Grassi (1887) and others to be the same species as that found in the mouse. In 1920 Joyeux proved that in the case of this tapeworm no intermediate host was required, since both the larval and adult forms grew in the same experimental mammal, while Saeki in the same year showed by human feeding experiments that the human and mouse species were fundamentally identical. Braun (1883), Parona (1886), Grassi (1886), Ijima (1888) and Zschokke (1890) showed that infection with the fish tapeworm, *Diphyllobothrium latum*, was contracted through consumption of fresh-water fish. It remained, however, for Rosen and Janicki (1917, 1918) to demonstrate the complete life cycle of this parasite, which was found to pass its first larval stage in small copepods, *Cyclops* and *Diaptomus*, before its passive entry into the fish along with the first larval host. Following this discovery Okumura (1919) showed that Manson's tapeworm, *Diphyllobothrium mansoni*, also utilized *Cyclops* as a first intermediate host, but that frogs and snakes served as the second intermediate hosts, conveying the infection to mammals.

Four of the nematodes parasitic in man, *Ascaris lumbricoides*, *Enterobius vermicularis*, *Trichocephalus trichiurus* and *Dracunculus medinensis*, were listed by Linnæus in his Systema Naturæ (1758–1767), while Gmelin recorded *Metastrongylus elongatus* in 1789 and Rudolphi described *Hæmonchus contortus* in 1803 In 1843 Dubini first described the hookworm, discovered by him in 1838 at the autopsy of a Milanese woman. In 1846 Leidy discovered *Trichinella spiralis* in pork, the first record of its presence in a host other than the human subject Bancroft (1876–1877) first recovered the adult filaria worm, *Wuchereria bancrofti*, from a lymph abscess of an arm and from hydrocele fluid of patients in Brisbane, Australia, although the microfilarial embryo of this species had been known for several years.

Sir Patrick Manson made the first epochal life-history contribution to the nematode group, by demonstrating (1878–1879) that the mosquito served as the larval host of Bancroft's filaria, and that the periodicity of the microfilariæ of this species in the peripheral blood of man appeared to be related to the life cycle Fedtschenko (1869) showed that *Cyclops* was probably the intermediate host of *Dracunculus medinensis*, a view later verified by Manson (1894) and by Leiper (1907) Leuckart (1882) proved that the parasitic and free-living generations of the human *Strongyloides*, namely *S. intestinalis* and *S stercoralis*, were part of the same life cycle In 1881 Perroncito published his findings on the development of the free-living larvæ (rhabditoid and filariform stages) of the hookworm, while Leichtenstern (1886–1887) claimed that the mature larva was capable of developing into the adult worm in the human intestinal tract Complete demonstration of the life cycle of the hookworm was first accomplished by Looss (1896–1911), who showed that the matur

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Western Hemisphere was different from that of the Old World species, and in 1903 gave it the name *Necator americanus* Recent work by Fulleborn and by Yokogawa (1925) and many other investigators has further elucidated the life cycle, while Cort and his co-workers have carried out most important work on the biology and epidemiology of the hookworm Davaine (1863) first observed that *Ascaris* larvæ hatched from eggs fed to experimental rats Lutz (1888) and Epstein (1892) demonstrated that the swallowing of the mature embryonated egg of *Ascaris* resulted in the development of mature worms In 1916 Stewart showed experimentally that the rhabditoid *Ascaris* larva, which hatches from the embryonated egg introduced into the digestive tract, migrates through the tissues Ransom and his colleagues (1920–1921) and Yokogawa (1923) not only verified this work of Stewart but also conclusively demonstrated that only one host is required for *Ascaris* Moreover, Ransom and Cram proved that these larvæ utilized the portal veins or the lymphatics *en route* from the intestines to the lungs Finally, Cort and Otto, as well as other workers, have provided fundamental information on the epidemiology of human ascariasis, especially among young children in the southern United States

MODERN TRENDS IN HELMINTHOLOGY

During the last decades epidemiological studies on hookworm disease, looking towards its eradication, have been undertaken on an extensive scale by various agencies, particularly the Division of International Health of the Rockefeller Foundation cooperating with various governments These investigations have included studies throughout the Tropics and Subtropics on the incidence of the infection in individuals and in populations, refined methods of technic for determining the degree of infections in individuals (worm-count, brine floatation and egg-

count) and the amount of infestation in the soil (Baermann technic); improved therapeusis (*e. g.*, administration of carbon tetrachloride, of carbon-tetrachloride-chenopodium mixtures, and later of hexylresorcinol and related drugs on a large scale), as well as the application of treatment to large groups (mass therapy); and finally on the biology of hookworm disease in the field (Cort and his colleagues).

The first steps in the scientific study of the helminth groups consisted in the description and classification of species. Later the subject of comparative morphology and relationships occupied the attention of investigators. With these more elementary but essential facts as a foundation, life-history data were then accumulated. While much remains to be done in each of these lines of investigation, the more pressing problems for the future involve the practical application of the information recently acquired, namely the relative pathogenicity of various species of human helminths, the number of individuals required for a clinical infection, improved methods of detecting the presence of helminths, particularly during the period of incubation, improved therapeusis, and, what is more important, the application of biological and epidemiological data to the control and eradication of these infections.

Most recent of all have come the intensive studies on host-parasite interreactions, with especial attention to host-resistance and immunological relations. Although some studies have been conducted along these lines on the flatworms (trematodes and tapeworms), for the most part the roundworms have constituted the special subject of investigation. Among the noteworthy contributions have been those on the hookworms, *Strongyloides*, *Ascaris* and *Trichinella*.

CHAPTER III

THE NOSOGEOGRAPHY OF HELMINTHIC INFECTIONS, WITH SPECIAL REFERENCE TO INFECTIONS OF MAN

GENERAL CONSIDERATIONS

In addition to the immediate environmental factors to which the helminth has become adapted as a parasite and on which, to a very great extent, it is constantly dependent, it is fundamentally important to have reliable information concerning the distribution of the organism over the surface of the globe, or its *nosogeographic range.* Until recent years it was commonly believed that human helminthic infections were limited almost [illegible] perhaps the most favorable regions for the propagation of parasitic infections, many of the most important helminth parasites have a wide distribution in temperate regions and that some even extend into the frigid zones. Some important helminths of man, as *Diphyllobothrium latum* and *Trichinella spiralis,* rarely occur indigenously in hot climates.

The most serious helminthic infection which is limited almost exclusively to the Tropics and the adjacent subtropical belts is hookworm disease, which, broadly speaking, completely encircles the inhabited regions of the globe between 20° N. and 20° S latitude. Yet even in this case there are numerous endemic foci, principally in mines, as far north as 50° N. latitude Furthermore, it has been found that *Necator americanus* is more strictly a tropical or subtropical parasite than *Ancylostoma duodenale,* which has its optimum habitat in a somewhat cooler zone, while *Ancylostoma caninum,* the dog hookworm, flourishes in an even colder climate.

Unlike many of the vertebrates, arthropods and molluscs, the distribution of parasitic helminths is rarely coincident with faunistic areas *Ascaris, Trichocephalus* and the majority of the human tapeworms are practically cosmopolitan in their distribution. Schistosomiasis hæmatobia and *Dracunculus* infection are both African and Oriental; schistosomiasis mansoni is African and Neotropical; schistosomiasis japonica is confined to the Sino-Japanese area of the Oriental region, as is also *Clonorchis* infection

DISTRIBUTION OF HELMINTHS DEPENDENT ON THE DISTRIBUTION OF THEIR HOSTS

A careful study of the problem shows that, in addition to climatic considerations, helminths are widespread or limited in their distribution, depending to a very great extent on the distribution of their hosts. Thus, infections requiring no host other than man and those requiring intermediate or reservoir hosts usually associated with man, such as the ox, the pig, the dog, or the rat, are nearly as widespread as is the human population itself, while those requiring a special type of intermediate host, such as a

mollusc with limited distribution, are limited to the distribution of this particular host. Some molluscs are fairly cosmopolitan in their distribution, others are very restricted in their range. Thus, the widespread distribution of species of *Lymnæa* throughout the moist temperate zones is no doubt responsible for the common occurrence of *Fasciola* infection in practically all areas into which the disease has been introduced in infected sheep. On the other hand, *Schistosoma japonicum* is adapted to a peculiar group of molluscs of limited distribution in the Sino-Japanese areas, so that its establishment in the other regions is very improbable.

CLOSE DEPENDENCE ON PHYSICAL SURROUNDINGS

In many cases the slightest deviation in the physical surroundings of a given geographical area or in the customs of the population may be responsible for an epidemic helminthiasis. In the time of Moses, the water supply of the Hebrews became poor in the desert of Hor, where they were encamped; they drank water from drying pools and ditches and became infected with a plague of *Dracunculus medinensis*, the Medina worm, the larvæ of which some transient Arab had previously left in the pool when he stopped by the wayside to bathe his ulcerated arm or leg. In this same way the epidemic of hookworm broke out among the construction gangs who were digging the St. Gothard tunnel, where the moist warm earth was favorable for development of the larvæ. In this same way pork tapeworm became a pest in parts of Germany fifty years ago, because the inhabitants were fond of eating raw pork flesh. Likewise, the broad fish tapeworm was introduced into the lake districts of Northern Minnesota, Michigan and lower Canada by the Scandinavian and Polish immigrants, who had perpetuated in their new homes the insanitary cycle to which they had been accustomed in Europe. Moreover, a single change of the topography of Lower Egypt, namely, the introduction of irrigation projects in the Nile delta, was responsible for the spread of schistosomiasis (bilharziasis) in that territory within recent decades.

Moisture is a *sine qua non* for the majority of helminthic infections. *Fasciola hepatica* not only requires snails and sheep but also moist pasture land *Clonorchis* requires snails and fish, which are in turn dependent on moisture. *Paragonimus* requires snails and crabs, which are both aquatic hosts. The schistosomes are dependent on an aquatic medium for their transfer to man as well as for the infection of their molluscan hosts. The hookworm and *Strongyloides* utilize no intermediate host but demand moisture and shaded warmth during their free-living phases. Only those forms in which there is essentially an anus-to-mouth transfer of the infective stage of the parasite, as in *Enterobius vermicularis* and *Hymenolepis nana*, or in which the transfer from the intermediate to the definite host is direct (*i. e.*, the intermediate host is the food of the final host) and in which the definite host or its excreta immediately reach the larval host, are independent of a continuously moist environment.

Moisture results primarily from rainfall, which in turn is dependent upon the winds, and upon the topography of the country, particularly the mountain systems near the sea. It is also dependent on the absolute temperature due to latitudinal position on the earth. Thus, on the island of Vitilevu of the Fijian group, a mountain chain prevents the rains, which the trade

winds from the southeast precipitate on that side of the island, from reaching the northwest side. Ancylostomiasis on the wet side rises to 90 per cent of the native and Indian population, while a similar population on the drier side has only a 38 per cent infection. Strongyloidiasis is even more limited than ancylostomiasis to warm moist regions of the globe, because the free-living larvæ of the parasites are very sensitive to drought. Trichocephaliasis is also much more common in moist than in dry areas. Schistosomiasis japonica exists only in those areas where the banks adjacent to the drainage canals are moist.

High inland plateaus or inland areas, shut off from adjacent moist regions by mountain chains, are invariably dry and the helminthic fauna of such regions is proportionally reduced, consisting among the indigenous non-migratory animals of nematode species in which the eggs are resistant to considerable desiccation and of cestode forms in which the larvæ have a direct transfer from definitive to larval host and back again to definitive host.

The monsoons of the Indian Ocean and the adjacent bodies of water, coming from the southwest and proceeding up the Arabian Sea, the Bay of Bengal and the China Sea, have a marked effect on the Asiatic Continent as far inland as the Himalayas. As one proceeds from the coast first in contact with the monsoons, where precipitation is heaviest, travelling northward and inland, he reaches territory where the rainfall is both less extensive in duration and less intensive in daily amounts. The helminthic fauna of these regions is usually directly proportional to the amount of precipitation. Thus, it has been found that in China hookworm infection is not clinically important north of the Tsing Ling Range (between the Huai and Yellow Rivers), where the annual precipitation is less than 75 cm.

In countries where there is intensive dry heat in summer (up to 125° to 150° F., or 57 to 71° C., in the sun) and bitter cold in winter (−40° to −60° F., or −43 to −55° C.), such as one finds in Siberia, the conditions are most unfavorable for the growth of most species of helminths. Where the summer climate is hot and humid, with adequate or luxuriant vegetation, such as one finds in the Tropics and Subtropics, and where the winter climate is also warm and moist, such as is found in the Malay Archipelago, the islands of the Caribbean region, and other countries where at sea level the average yearly temperature is between 75° and 85° F., or 26° and 32° C., optimum conditions exist for the helminth's development.

HYGIENE AND SANITATION IN RELATION TO HELMINTHIC INFECTIONS

With these broader, more general conditions of the environment in mind, attention may now be directed to other external agencies which control the development and distribution of helminthic infections. Among the many factors other than meteorological that govern the dissemination of helminthic infections and their incidence in man the following may be mentioned:

1. Food
2. Drinking water.
3. Human excreta
4. Migration and travel.

This list is not exhaustive. The factors named are not necessarily arranged in the order of their importance, nor are they separate and distinct from one another. Certain of these factors are of historical importance only. Others are known or determinable entities which may be of primary importance in the control of the infections as they now exist.

1. **Food.**—The *food of a people is always an important point of attack* in attempting to discover the etiology of an infection and in establishing preventive measures for its eradication. For example, the Chinese and Hindus thoroughly cook the greater part of their food. A considerable part of this is eaten while hot. Yet some of it is allowed to stand uncovered in stalls and restaurants for a considerable time before it is consumed, during which interval it is exposed to dust and dirt, flies and domestic animals. Still other foods are eaten raw, particularly vegetables, molluscs, crustaceans and fish. Generally speaking, foods grown in the ground, where human night-soil is used as fertilizer, are all more or less contaminated. *Furthermore, in order to keep these vegetables in a fresh condition* in the markets, the bazaar venders sprinkle them with brooms which have [illegible]. This is particularly true of such [illegible] water chestnut, lotus roots, sugar cane and bamboo shoots, all of which the Oriental enjoys eating uncooked. Oranges which have begun to wither are given a hypodermic injection of water to improve their sale. Melons and cucumbers are only less likely to be the source of helminthic infection in Oriental and tropical countries than of protozoan and bacterial contamination. For those individuals in Oriental or tropical countries who eat fresh celery and lettuce a source of contamination is ever present. In China and India the water chestnut and the red water-ling, the so-called "buffalo nut," are means by which *Fasciolopsis* infection is conveyed. The encysted larval fluke adheres to the skin of the corm and the outer shell of the nut, so that in peeling off the skin or shell with the teeth and lips some of the cysts get into the mouth and thence reach the intestine, where the cyst wall is digested away and the larval worms grow to adult form. In other regions of China, as in Formosa, perhaps the infection is also conveyed by eating herbs or grass. It is common knowledge among the farmers of Central China, where the infection occurs in hogs as well as in man, that animals kept in the courtyards do not get the infection, while those that pasture on the hillside or in the fields sooner or later contract the infection. Similarly, cattle which are fed on dry hay are less likely to acquire *Fasciola* infection than those allowed to graze in infected marshy meadows. In Mediterranean and Latin American countries human exposure to sheep liver-fluke most frequently results from eating water cress as raw salad.

The Chinese people as a rule differ from their immediate neighbors around the China Sea in not eating fish or arthropods in the uncooked state. They should, therefore, be free from the common fluke diseases of the Japanese, Koreans, Formosans and Tonkinese, acquired through the consumption of such food, namely clonorchiasis, metagonimiasis and paragonimiasis Nevertheless, in South China and to a certain degree in Central China these foods are eaten raw either by preference of through ignorance of their harmful effects, and fluke infection results.

2. **Water.**—Water in all tropical and Oriental countries is always subject to suspicion, not only for drinking but also for bathing purposes. Vasilkova (1944) has reported that the effluent from the sewerage of Moscow emptying into the river of the same name contained eggs of *Ascaris, Trichocephalus, Tænia, Diphyllobothrium, Enterobius* and *Dicrocœlium*, amounting to 4,500 per cubic meter. Even where there is no danger from typhoid, cholera and bacillary or amebic dysentery, the cercariæ of the human blood flukes are found in quiet pools, canals or irrigation projects over so large a portion of Africa, Latin America, the Near East and Middle East, and the Far East as to make bathing, wading or washing clothes in such waters extremely dangerous. The incidence of "bilharziasis" among the Australian troops in Egypt during World War I, of American and Australian troops on Leyte in the Philippines from October, 1944 through the spring of 1945 and the common occurrence of Oriental schistosomiasis among farmers, boatmen and foreign sportsmen in the Yangtze valley are outstanding instances of such danger. Furthermore, raw drinking water in endemic areas is the source of dracontiasis and possibly of sparganosis.

3. **Human Excreta.**—Without doubt the most potential source of human infection with the common helminths is that of human excreta, resulting from propensity of human beings to pollute their surroundings. No dogmatic statement concerning the actual percentage of cases of infection which this provides can be made, since in the first place conditions of disposal of night-soil vary tremendously in various parts of the world; and in the second place almost nothing is known about the viability of eggs, cysts and larvæ in night-soil during the time it is kept and prepared for manurial purposes, although the work of Winfield (1937) in Shantung Province, China, on the epidemiological relationship of human excreta and ascariasis constitutes a notable exception Contrary to common belief, the use of human excreta for fertilizer is not confined to Oriental countries but is practiced extensively in the Mediterranean area, and is not unknown in the Western Hemisphere, including truck gardens in the United States.

4. **Migration and Travel.**—Hookworm (*Necator americanus*) and *Schistosoma mansoni* are believed to have been introduced into the Western Hemisphere through the importation of negro slaves from the Gold Coast and Mozambique. The former required no adaptation; the latter found an appropriate intermediate host in the mollusc, *Australorbis glabratus*. The Medina worm (*Dracunculus medinensis*) and the loa worm (*Loa loa*) were also probably disseminated by transportation of slaves (Scott, 1943). Mention has already been made (*vide supra*, this chapter) of the introduction and establishment of *Diphyllobothrium latum* infection by immigrants from Northern and Eastern Europe into North America. Darling has shown how the Punjabis and Chinese immigrants to Malaya and Micronesia have altered the hookworm index of these countries by the introduction of *Ancylostoma*, while European immigrants to Brazil have superimposed *Ancylostoma* infection upon that of *Necator*. Chinese returning from the Malay States and the South Seas have introduced *Necator* into South and Central China, while travel between these regions and North China is carrying it temporarily beyond its optimum temperature range Wherever the Mohammedan religion has spread, *Tænia solium* has ceased to become an important disease but *Tænia saginata* has become hyperendemic.

Nevertheless, migration and travel cannot be held entirely responsible for the apparently greater distribution of helminthic infections today than the known distribution a quarter of a century ago. Much is due to our more adequate knowledge of the subject, particularly to surveys and investigations within recent years. Thus van Beneden, writing in 1889, stated that the broad tapeworm occurred only in Russia, Poland and Switzerland; that *Hymenolepis nana* has been observed nowhere except in Abyssinia; that *Ancylostoma* was known only in the south of Europe and the north of Africa; that the dracunculus was believed to occur only in the east and west of Africa, and that "the Bilharzia, that terrible worm, had only been found in Egypt." A comparison of such data with those available at the present time for these and other helminths indicates how rapidly knowledge of the subject has developed. Even recently the more refined methods for the diagnosis of *Trichinella* infection in man have demonstrated that a considerable proportion of individuals coming to autopsy in the United States without apparent history or symptoms of trichinosis actually harbors light *Trichinella* infection.

5. **Other Factors.**—Man-made breeding places for Arthropod transmitters of helminthic infections have also contributed to the establishment and perpetuation of these diseases. Domestic mosquitoes and Bancroft's filariasis, as well as filth flies and ascariasis, constitute notable examples. Likewise, rats and other reservoirs have been "invited" to breed around human habitations. Moreover, contact with infected natives has at times provided appropriate opportunity for the exposure of new population groups.

Thus we find, that environmental factors, whether they are the more general conditions of climate and topography or the more specialized ones of the parasite and its host to the immediate setting, all play important parts in the propagation and dispersal of helminthic infections.

CHAPTER IV

THE INTERRELATION OF THE HELMINTH PARASITE AND ITS HOST

PARASITE AND HOST ADAPTATIONS

THE host as the organism which houses and provides food for the helminth is a *sine qua non* for the latter's existence. No matter how much of its life cycle is of a free-living character, the remaining part which necessitates a host is of vital importance to the parasite and possibly to the host. To the parasite, parasitism means first of all the immediate presence of the particular host to which the parasite has become adapted. This intimate interrelationship is referred to as *host specificity*. Furthermore, it involves the ability of the helminth to secure entry into the host through the proper channel, and, finally, after reaching the appropriate residence in the host, to secure nourishment without endangering the life of the host and hence its own security. On the other hand, certain parasites, which are incompletely adapted to residence in certain hosts, are able to take up existence in these hosts when malnutrition lowers their threshold of resistance. To the host, parasitism means the physical burden of the helminth's presence in the body, the frequent injury of its tissues, due to migration of the parasite or abrasive action of its hooks, spines, or other organs of attachment and penetration, and, what is even more serious, the toxic effect of the products secreted or excreted by the parasite and absorbed into the tissues of the host

The adaptation of the helminth to certain particular species of hosts is a condition that has gradually developed over a long period of years. It has undoubtedly come about from the continual coexistence of the helminth and a particular species of host in the same habitat, assuring the helminth the constant availability of such a species under ordinary conditions. The presence of the host in a particular habitat depends on many external factors, among which may be mentioned the general climatic conditions, including temperature and moisture, edaphic (*i e.*, local) factors, and the general distribution of that particular species of host over the surface of the globe and its ability to withstand climatic and edaphic changes. The presence of the parasite in the same habitat is largely fortuitous, depending in many cases on the movements and specialized habits of the previous host which carried the parasite about and deposited it for a longer or shorter period of free existence before it was obliged to seek entry into another host.

In the case of many helminth parasites, entrance into the appropriate host is also largely fortuitous. Such instances usually depend on the host ingesting the appropriate stage of the helminth along with food or drink, or the active entry of the parasite into the skin. The oral route of infection obtains in the case of *Enterobius*, *Ascaris*, *Trichocephalus* and certain other nematodes requiring only one host, in which the fully embryonated eggs of the worm gain access to the host as a contamination. Such is also the ordinary method by which many tapeworms gain entry into their respective

hosts. While two or more alternate hosts are required, the eggs of the parasite are usually swallowed by the intermediate host; this host, together with the larvæ of the parasite, which have developed from the ingested eggs, later becomes the food of the final host or second intermediate host, as the case may be. Such is the method by which the human flukes, *Clonorchis*, and *Fasciolopsis*, gain entrance to their human hosts, namely, after encystment of the larvæ in or on food consumed by man.

Other species of helminths, including certain nematodes and all of the blood flukes parasitic in man, gain access to at least one of their hosts in an active way. In the case of the hookworm and of the blood fluke, human infection results from the activity of the mature free-living larval form, once it has come in contact with the human skin, in penetrating through the layers of the skin into the softer tissues of the body, whence it continues its migration to the seat of its adult residence in the body. This type of invasion is probably conditioned by a tactic reaction, being an attempt to avoid desiccation. Furthermore, the miracidium, which hatches from the trematode egg, and the cercaria or tailed larva which emerges from the molluscan host after the intermediate phases of the life cycle of the trematode have been completed, are both free-swimming organisms and were originally, at least, active invaders of the hosts which they next utilized. This type of penetration requires a selection of the proper host. At first the parasite probably attempted to attack at random all objects in its immediate vicinity, but later became adapted to a particular species of organism, which it was able to select by becoming adjusted to a particular chemotactic stimulus. At least three types of flukes, parasitic in man, *Clonorchis*, *Heterophyes* and *Dicrocœlium*, the miracidia of which are provided with a ciliated epithelium and organs for penetrating host tissue, have lost their use of this free-living phase of the life cycle, since their eggs never hatch naturally until they are ingested by particular species of molluscs. In both the miracidial and the cercarial stages of digenetic trematodes there are digestive glands, with openings around the oral end of the larva, which secrete a histolytic substance helpful in dissolving the tissues of the host through which a path of migration is opened.

Joyeux (1944) has summarized the host species adaptations of the more important helminths of man as follows: *Fasciola hepatica*, wide adaptation, although found primarily in ruminants; *Clonorchis* and *Opisthorchis*, parasites of carnivores in contact with man; *Fasciolopsis buski*, possibly two races, one human and one porcine; Heterophyidae, with wide adaptations; *Paragonimus westermani*, with moderately wide adaptation to carnivores eating raw crabs and crayfish; *Schistosoma japonicum*, with wide adaptations; *S. mansoni*, rarely a natural parasite of hosts other than man; *S. haematobium*, a natural parasite of man only; *Tænia solium* and *T. saginata*, became adapted to man when he developed carnivorous habits, probably during Glacial Age when vegetation became scarce; *Bertiella studeri*, primarily simian; *Hymenolepis nana*, a human variant of the murine species *H. fraterna; Ascaris lumbricoides*, developed from the hog *Ascaris; Trichocephalus trichiurus*, a parasite of man, monkeys and the hog; *Necator americanus*, originally African, presently parasitic in man, various monkeys, rhinoceros and the Brazilian rodent, *Coendu villosus* (de

Almeida, 1934), not identical with *Necator suillus* of hog; *Ancylostoma duodenale*, adapted to man, monkeys, wild carnivores, occasionally hogs; *A. braziliense*, parasite of carnivores, only partly adapted to man; *Strongyloides stercoralis*, man, dog, cat, chimpanzee; *Trichinella spiralis*, with wide adaptation; *Wuchereria bancrofti*, man only; *Loa loa*, with extensive simian adaptation; *Onchocerca* spp., with three types of hosts, horse, ruminants, man, phylogenetic lineage uncertain; *Dracunculus medinensis*, with wide host adaptations.

Once the helminth has reached its residence in the definitive host, its primary concern is to secure nourishment. For this purpose it has usually chosen a position where digested or semi-digested food is abundantly supplied. Some worms are capable of secreting digestive ferments, which aid in the digestion of the host's tissues before these are taken into the body of the parasite. Adult worms living free in the digestive tract of the host may wander back and forth as they require. Others which are attached more or less securely to the intestinal wall may release their hold and secure a more favorable one farther along. Thus, in heavy hookworm infections, [illegible] obtained a new one in the intestinal mucosa, the latter being always progressively farther down the gut. *Clonorchis* does not normally leave the bile tracts once it has migrated into them, but it may wander about in the bile capillaries. If this worm is expelled into the intestine it is usually digested at once.

Most of the parasitic helminths are capable of resisting the digestive action of the host's juices and tissues by the secretion of anti-enzymes. The blood flukes are confined to the mesenteric portal system, except that they may occasionally escape into the vena cava *via* the median and inferior hemorrhoidal vessels. Their eggs escape into the lumen of the intestine (*Schistosoma mansoni*, *S. japonicum*) or into the bladder (*S. hæmatobium*) by rupture of the venules into which they have been forced. Bancroft's filaria (*Wuchereria bancrofti*) is blocked in lymph channels, but the microfilariæ gain access to the circulating blood. The Medina worm (*Dracunculus medinensis*) lives in the visceral and subcutaneous tissues of man, but the female worm, stimulated when she is gravid with embryos, emerges to the surface and deposits her larvæ in the water when the host washes the infected member of his body in a pool or ditch, thus providing an opportunity for the larvæ to reach the alternate crustacean host which lives in the water.

The metabolic processes of parasitic worms have not been adequately studied and are, for the most part, poorly understood. This has been due primarily to difficulties experienced in studying the strictly parasitic stages under experimentally controlled conditions. There is cumulative evidence, however, that species living in the intestinal tract of man and higher vertebrates tolerate a relatively wide range in the pH of the medium; that they live optimally under anaerobic or semianaerobic conditions, and that they require a considerable amount of soluble carbohydrates, preferably monosaccharides, which they absorb and store in the form of glycogen

Some parasitic helminths ingest red blood cells, utilizing the globin and depositing the undigested iron in the form of hematin. Information is accumulating that certain vitamins are required for satisfactory growth. The subject will be considered in greater detail under each group for which there is sufficient information.

An adaptation which is optimum for the parasite requires that the host be not overburdened by the presence of the parasite nor that its life be endangered. Where the parasite has reached an equilibrium with its host, there are few, if any, symptoms of disease. On the other hand, parasites which may be temporary residents in a host but cannot readily become adjusted to permanent residence, as, for example, the human *Strongyloides* in the dog, and other forms which have an even less specific host-parasite adjustment, such as the dog hookworm, *Ancylostoma caninum*, in man, and the human hookworm, *Necator americanus*, in the dog, are also of little clinical interest. In a somewhat different category is the case of the human and pig *Ascaris*, and possibly the dwarf tapeworm of man and the rat, which, in each case, are morphologically indistinguishable but which have specific physiological adaptations for their respective hosts. Likewise, the diet of the host is closely related to the ease with which the helminth is capable of adapting itself to a relatively specific host. In a well-nourished host the resistance is high and the parasites maintain their position with difficulty. In poorly-nourished hosts the reverse is true. Between the perfectly adapted parasites on the one hand and the entirely non-adapted ones on the other there is a wide range of ill-adapted species, whose relationship to the host produces a reaction of the tissues which the pathologist and the clinician look upon as disease.

[illegible] a consider-
[illegible] produce a
[illegible] or *Taenia saginata* may at times cause severe anemia. Again, a single worm may obstruct a channel through which body fluids pass and bring about morbid reaction of the host. Such, for example, is the case when a filaria worm obstructs a lymph channel or an *Ascaris* blocks the common bile duct. Some worms in small numbers (*Clonorchis, Trichocephalus, Necator*) produce very mild reactions on the part of their host, while in large numbers they are of clinical significance. Some worms, like the hydatid cyst, may grow to such size that they press upon contiguous organs and bring about dysfunction. In other species of helminths (*Schistosoma*) the eggs of the worm infiltrated into the surrounding tissues produce a diseased condition much more profound than do the adult worms. In blood fluke infections not infrequen [illegible]
its metabolic [illegible]
and metastas [illegible]
of the host than the helminthic infection *per se*. Such abnormal tissue proliferation, stimulated by helminths, is well illustrated in infections of the rat, as cysticercosis fasciolaris and gongylonemiasis. This entire subject has been carefully studied and admirably presented by Hoeppli (1933).

Some helminthic infections are significant in childhood and apparently

decrease in their pathogenicity as the host matures In one infection at least (*Hymenolepis nana*) the worm lives almost exclusively in children, and is much less common in adults. In infections with *Ascaris*, hookworms and *Hymenolepis nana* age resistance plays a very important rôle.

While all members of the human species appear to be equally susceptible to infection with helminth parasites, races of man, or even special communities, which have been long subjected to these infections, appear to be more adapted to the parasites involved than those in which the infection is relatively new. Thus the Negro is less seriously affected by hookworm infection than the Anglo-Saxon, the Chinese child appears to be less disturbed by the presence of *Ascaris* in the bowel than does the Anglo-Saxon, and a single infection with a blood fluke assumes a mild chronic form in the native population of endemic areas more commonly than in the foreigner. It is not unlikely that relative age and racial resistance, or even immunity, may be due to light infections acquired early in life, and that specific antibodies developed by the host's tissues are primarily responsible for such resistance. (*Vide* Bachman, 1938.)

Enough has been said in the foregoing paragraphs to explain how the parasite has become associated with certain hosts and how the general process of adaptation is going on, how, in some cases a nearly perfect adaptation has been effected; how, in others, there is still no true adaptation at all; while in a very large series of cases poor adaptations exist, resulting in disease. In a broad biological sense, given contact of a host species with a pathogenic helminth for thousands of years, changes resulting in the equilibrium of the host and the parasite, with a corresponding reduction in pathogenicity, might be expected, and this undoubtedly has been the case

TYPES OF HOSTS IN RELATION TO VARIOUS STAGES IN THE LIFE CYCLE OF HELMINTHS

Considering the host-parasite relationship from a different viewpoint, certain terms which define this relationship occupied by the host in the life cycle of the organism have come to be accepted through common usage. This phase of the problem has both a biological and an epidemiological bearing. The host in which the adult hermaphroditic or diecious helminth develops is referred to as the *definitive host*. Thus, the large intestinal fluke (*Fasciolopsis buski*), the blood fluke (*Schistosoma japonicum*), the adult beef tapeworm and the adult hookworm are all harbored by their definitive host

If another organism serves as a reservoir of such an infection and preserves the continuity of the life cycle of the parasite when man escapes infection, this host organism is known as a *reservoir host*. In endemic areas the pig frequently serves as a reservoir host for *Fasciolopsis*, and the dog for *Schistosoma japonicum*, and to a lesser degree for *Strongyloides stercoralis*, while no reservoir host is known for the beef tapeworm. On the other hand, both the dog and the cat are reservoir hosts of *Ancylostoma braziliense*, an occasional hookworm parasite of man In *Trichostrongylus*, *Triodontophorus*, *Gnathostoma*, *Gastrodiscoides* and *Fasciola* infections, domestic or wild mammals are the common reservoirs of infection and man is a relatively

incidental host. Human infection with *Gnathostoma* usually differs from that of the common reservoir hosts, the dog, cat (*G. spinigerum*) and pig (*G. hispidum*), since in man the parasite is almost without exception found as an immature worm in the subcutaneous tissues, while in the more perfectly adapted hosts the worm matures in gastric tumors. At times mature larvæ, as, for example, those of the spiruroid nematodes, are ingested by an inappropriate host. Under such circumstances the larvæ may burrow through the tissues and become encapsulated there or in body cavities.

For some helminth parasites the definitive host is the only one utilized. In the case of *Ascaris* and the hookworm a larval migration period through the body tissues is normally required before the parasite settles down and grows to adulthood. In such instances, however, man cannot be referred to as a true larval host. Such a host, spoken of as an *intermediate host,* is one alternating with the definitive host in the life cycle of the parasite. Thus, the ox is the intermediate host of the beef tapeworm, the mosquito is the intermediate host of Bancroft's filaria, and the mollusc, that of the blood fluke. In echinococcus infection the dog is the definitive host in which the adult worm lives, and man, the ox, the sheep and the pig are the usual intermediate hosts in which the larval stage (hydatid cyst) develops. In the case of *Trichinella spiralis*, the rat, the hog and man may serve both as definitive and intermediate hosts. The adult worms develop in the intestine (definitive stage) and the females discharge their larvæ into the blood or lymph spaces, from which they migrate to the muscle layers and encyst (larval or intermediate stage). The infected flesh, when eaten by the next host exposed, produces the definitive stage again, and thus the cycle is carried on.

The mollusc is an obligatory intermediate host of all digenetic trematodes. The parasitic progeny developing within the mollusc (two or more stages) are regarded by some investigators as the products of parthogenesis, by others as the result of polyembryony, and by still others as strictly asexual in their development. After the cercaria emerges from the mollusc and discards its tail it is spoken of as the *metacercaria.* Except for the blood flukes all of the human trematodes have a period of rest or incubation following development in the mollusc and previous to entry into the final host. If this involves a second larval host, as in *Clonorchis* infection, where a fresh-water fish is utilized, the mollusc is designated as the *first intermediate host* and the fish is known as the *second intermediate host.* In *Fasciola-*, *Fasciolopsis-*, and probably in the human amphistome-infections, the cercaria encysts on grass or other vegetable surfaces and is passively transferred to the human or reservoir host. Such a condition differs from that of encystment in the flesh of a fish, since in the fish an actual incubation or growth occurs, while the former is only a vehicle for the transfer to the definitive host. Vegetable tissue which serves such a function is, therefore, not a true intermediate host but a *mechanical vector.* In a broader sense flies may serve as, mechanical vectors for helminth eggs.

In his stimulating and well documented essay, "This Wormy World," Stoll (1947) has provided an estimate of the total helminthic infections

throughout the world which is both staggering and illuminating. It amounts to 2,257.1 million, or slightly over one infection for each living human being. In North America it is 0.31 per capita; in Tropical America, 1.38; in Africa, 2.10; in Europe, 0.36; in the U. S. S. R., 0.70; in Asia, 1.24, and in the Pacific islands, 0.34. Although the highest incidence is in Africa, the heaviest worm burden is in Asia due to the dense population.

CHAPTER V

PATHOGENESIS AND CLINICAL ASPECTS OF HELMINTHIC INFECTIONS

THE HELMINTH IN RELATION TO DISEASES OF ITS HOST

ALTHOUGH the term "*carrier*," that is, a host which shows no obvious symptoms of an infection, has come into use in connection with bacterial and protozoan infections, its use is still somewhat new in helminthology. There is no reason, however, why it cannot be applied equally well in human helminthic infections, such as ascariasis, trichocephaliasis, ancylostomiasis, enterobiasis (oxyuriasis) and hymenolepiasis nana, in which no intermediate host is required and in which an infected human being, manifesting no apparent symptoms, is a danger to the members of his community. In a more figurative sense reservoir hosts which are infected with helminths requiring an alternate host are also "carriers."

An interesting condition is found in the case of *Troglotrema salmincola*, a minute fluke parasitic in the mucosa of the small intestine of fish-eating mammals on the Pacific Coast of North America, and recorded from the aborigines of Eastern Siberia. The parasite *per se* produces a superficial enteritis and local necrosis of the tissues, rarely petechial hemorrhage. However, a filtrable virus, present in the immature flukes encysted in the salmon flesh, produces an acute infection, known as "salmon poisoning," in dogs and their wild relatives which consume the infected fish. Mortality in these hosts ranges from 50 to 90 per cent. Diagnosis is based on recovery of the eggs of the fluke in the feces of the host. Recovery confers lasting immunity to the viral disease, but not necessarily to reinfection with the fluke.

Helminthic diseases may become *epidemic* in nature, due to the introduction into an area of a particularly heavy infection, to exposure of a completely non-immune population group, or to unusually favorable climatic conditions for the parasite. More often, however, such diseases are *endemic*, the infection being maintained in a locality by a repetition of conditions or a correlation between parasites and hosts in such a way as to preserve the infection. Wherever such circumstances supervene, a *vicious cycle* is established. No better example of a complicated life cycle of this kind need be found than that of *Diphyllobothrium latum*, the broad fish tapeworm, which requires, *ad seriatim*, copepods, fresh-water fish and man or other suitable mammals as hosts.

The damage in the host's body as a result of the helminth's presence is frequently both local (*i. e.*, at the site where the worm is located) and systemic. Locally it may be traumatic, that is, mechanical, or it may be lytic, with digestion of host's tissues. Both of these types of destruction may take place during the migration of the parasite through the tissues of the host or later after the worm reaches its adult location. Examples are provided by *Ascaris* larvae as they break out of the pulmonary capillaries

into the air sacs, by *Schistosoma* metacercariae which reach blind ends in blood capillaries, and by maturing and adult hookworms attached to the intestinal mucosa.

The metabolites of the worms, both secretions and excretions, frequently provoke local and systemic reactions on the part of the host. In the absence of bacterial or other supervening infections, in many helminthic infections there is typically an acute or subacute local inflammatory reaction, in which eosinophils, lymphocytes, histiocytes, epithelioid cells and giant cells predominate over neutrophilic leukocytes. This usually leads to an eventual fibrosis of the area, in an attempt to wall off the parasite, its eggs or larvae. The systemic reaction is frequently one of toxemia, causing a general malaise, a variety of nervous symptoms and at times an anemia. Whenever there is pronounced local eosinophilia, there is characteristically a comparable relative, or possibly absolute, increase in the proportion of these cells in the circulating blood. This is a sign of host's sensitization to the foreign substances being elaborated by the parasite. While this reaction varies widely in different hosts of the same species, as a rule it is most consistently conspicuous in those infections in which the parasite has intimate contact with the host's tissues, either in migration during the incubation period or later. This sensitization may produce such allergenic phenomena as giant urticaria, asthma or even an eclamptic state.

Following the acute reactions to the parasite a chronic stage ensues, in which fibrotic encapsulation of the intruder and its eggs or larvae characteristically occurs, providing a certain amount of tolerance on the part of the host. At this stage, there is usually a relative monocytosis as in other infectious processes, with a reduced eosinophilia. If, however, death of the parasite suddenly occurs without its adequate encapsulation, there may be a dramatic generalized sensitization reaction, as, for example, in Bancroft's filariasis, cysticercosis cellulosae and hydatid infection. Certain helminths, as species of *Schistosoma*, have a long expectation of life and their continued vitality tends to keep the host sensitized. Moreover, fibrotic repair of host's tissues replacing functional cells, frequently causes blockage or space-occupying masses which seriously affect normal physiology.

At times the lesions produced by helminths allow bacteria and other micro-pathogens to gain entry into the tissues, thus complicating the condition A relatively common example is that of *Ascaris* causing perforation of the intestinal wall, enabling coliform bacteria to set up a peritonitis Another example is the indirect effect of filarial elephantiasis, in which the blood supply to the skin of the involved area is practically shut off, with thickened, cracking epidermis which permits streptococci, staphylococci and cutaneous fungi to enter and set up infection.

This brief synopsis of the host-parasite inter-relationship provides an orientation for the disease states which the clinician meets in the patient and for which he must make accurate diagnosis and then undertake appropriate therapy.

THE SYMPTOMS IN HELMINTHIC INFECTIONS

The signs and symptoms in helminthic infections vary quantitatively and qualitatively, depending on the number or mass of the parasite, its

position in the body, its longevity, the effect on the host produced by its eggs, larvæ and metabolites, and the tolerance of the patient to the particular infection. The symptoms may be those of an acute infectious disease, may be of moderate intensity, mild or essentially inapparent (*i. e.*, carrier state). They may be localized at the site of primary infection, at a distance from the characteristic location, or generalized. They may be syndromic or asyndromic. A few examples will serve to clarify these general statements.

An average, mature beef tapeworm (*Tænia saginata*), measuring 12 to 20 feet (about 4 to 6.5 meters) in length, fills a two to three liter container. Aside from the nutritional drain on the human body and the toxic metabolites absorbed, the mass of this worm in the small bowel is considerable. Yet it may produce no apparent symptoms. A ball of intertwined *Ascaris* in the same location is more apt to produce manifestations of an acute abdomen. A hydatid cyst pendant from the right lobe of the liver may develop to the size of a football with no pain and relatively little discomfort unless a sudden blow causes it to burst, with potential anaphylactic reaction. A small cystic mass or tumor in the brain or spinal cord will usually cause early symptoms and may possibly result in death. A pair of delicate filaria worms (*Wuchereria bancrofti*) in a groin gland or epididymal gland may provoke sufficient tissue reaction to result in extensive lymph varicosity or elephantiasis. Yet in many persons this infection is essentially asymptomatic. Occasionally in children a small number of the dwarf tapeworm (*Hymenolepis nana*), of the pinworm (*Enterobius vermicularis*) or of the whipworm (*Trichocephalus trichiurus*) are responsible for serious illness, while in other children many worms of these species appear to produce no appreciable difficulty.

Thus, it is necessary for the physician to evaluate the symptoms in the light of the average manifestations observed or reported for the infection and, at the same time, to keep in mind the likelihood of atypical manifestations Moreover, the symptoms present in the patient may be due only in part to the helminthiasis. Thus, the fundamental difficulty, as is so frequently the case in hookworm infection, may be a state of malnutrition aggravated by the parasites. Or there may be evidence of an intestinal or hepatic carcinoma with an associated helminthiasis, which may or may not be contributory to the diseased state. The clinician should be "parasite conscious," but this should not outweigh a balanced judgment based on a broad background of experience in the practice of internal medicine.

DIAGNOSIS AND THERAPY

The case history is frequently helpful in suggesting a tentative diagnosis of helminthic infections. Geographical location, the patient's routine habits, the customs of the particular population group and their sanitary status are all useful in providing clues. Added to these are the findings from physical examination and the signs and symptoms discovered on careful questioning. All of these provide the presumptive clinical diagnosis, which must be substantiated by demonstration of the parasite in one of its stages.

Since a majority of helminths are intestinal parasites, the stool is the most useful source of information, but in other infections the urine or sputum constitutes the medium for examination. At times biopsied or surgically-removed specimens contain the evidence required. In a number of instances immunological and serological tests are most helpful, provided the test antigens are sufficiently pure and diluted enough to prevent false positive reactions. The technics most practical in laboratory diagnosis of the common helminthic infections of man are presented in considerable detail in Section VII (*vide infra*).

Therapy in the helminthiases resolves itself into (1) general management and (2) anthelmintic medication. The former consists of general supportive measures to insure adequate catharsis or to alleviate excessive diarrhea (and thus control dehydration), to protect the liver, kidneys, heart and lungs, to maintain the constituents in the blood plasma at normal levels, and, above all, to provide a nutritious diet, fortified with vitamins, iron and occasionally liver extract, to combat malnutrition. Transfusions may be indicated in patients suffering from severe anemia. For certain types of patients it is desirable to carry out these supportive measures for a week to ten days previous to anthelmintic medication.

The available anthelmintics, their relative efficacies, contraindications and the management of the patient during the period of treatment are considered for each important helminthic infection in a special chapter in Section VII (*vide infra*).

CHAPTER VI

CONTROL OF THE HELMINTHIC INFECTIONS OF MAN—THE SCOPE OF THE PROBLEM

INTRODUCTION

CONTROL of any disease or group of diseases has as its goal the improvement of the health of the individual and of the community. Such an undertaking can not be properly conceived and entered into without accurate information, a practical program, an adequate staff and sufficient funds. The most notable program ever launched for the control of a helminthic infection is that on hookworm, initiated in the Southern United States in 1915 by the Rockefeller Foundation and later carried into practically every country in the World where the infection was prevalent. An examination of this project indicates the wisdom of effective cooperation [illegible] 'or [illegible] he [illegible] ch had to be considered before setting up practical control measures; the desirability of coördinating the services of clinicians, laboratory diagnosticians and public health officers in the area of control, and the need for educating the population as to the purposes of the program in order to obtain their support. While many helminthic infections are less extensive in their distribution and may be brought under control without so great an expenditure of effort and financial outlay, the lessons learned by the hookworm control program are, in many respects, applicable to other helminthiases of clinical and public health importance.

KNOWLEDGE OF THE POPULATION AND ITS ENVIRONMENT

Why are certain helminthic infections prevalent in one community or one country and not in a nearby area? The answer may be found in the customs of the people or in the environment. As an illustration of the human factor one may consider infection with the giant intestinal fluke, *Fasciolopsis buski*. In the Canton region of China this is a major clinical and public health problem, whereas in Fukien Province, only a few hundred miles to the north, human infection is uncommon. In Canton the "water chestnut" which is the plant vector, containing the encysted larvae on its surface, is "peeled" by using the lips and the teeth, the little cysts become free in the mouth, are swallowed and initiate infection. In Fukien a knife is used to peel off the inedible hull and no infection results. As an example of the environmental factor, differences in rainfall, topography, temperature, presence or lack of essential intermediate hosts and other epidemiological conditions may be responsible for heavy infection, light infection or complete lack of it.

RESERVOIR HOSTS AND CONTROL

When man alone is the definitive host of a helminth, the problem of control is far simpler than that in which there are efficient reservoir hosts. In

hookworm infection, strongyloidiasis, taeniasis and vesical schistosomiasis there are no good reservoirs of the infection to replace man in the cycle By controlling human customs it is possible, although not easy, to control these helminthiases. Likewise, in Bancrofts' filariasis, known only as a human infection, eradication of the mosquito intermediate host constitutes sound preventive practice. On the other hand, Oriental schistosomiasis, clonorchiasis and sheep liver-fluke infection defy control by eliminating human exposure, since there are numerous efficient reservoirs

CONCLUSION

In preventive medicine as applied to the helminth parasites of man there is need for a basic understanding of each disease entity in relation to the customs of the infected population and the environmental conditions which favor the propagation of the parasite. Prevention or control is impractical without general and particular epidemiological information concerning the parasite. Frequently the services of specialists, such as experienced parasitologists, medical entomologists, sanitary engineers, agriculturalists, visiting nurses, social workers, and at times anthropologists, must be enlisted to elucidate the background of the problem and to provide practical answers to the difficulties encountered in carrying out control.

CHAPTER VII

THE SCIENTIFIC NOMENCLATURE OF HELMINTH PARASITES

INTRODUCTION

UNDOUBTEDLY the most perplexing and most troublesome element entering into the study of any group of animals or plants is the scientific terminology or nomenclature of the various species. Of animal species it has been conservatively estimated that there are probably more than 10,000,000, of which only about one-tenth have been carefully described and named. To the medical zoölogist or the physician, who is primarily interested in the study of a parasitic organism in relation to its environment and the disease which it occasions in its host, the application of a set of rules, which appears to be arbitrary, and at the same time inconsistent, is irksome and cumbersome. As a matter of fact the rules which apply to zoölogical nomenclature may be arbitrary but they follow with the utmost consistency a code of procedure, based on the work of the physician Linnæus, and framed by a representative group of zoölogists, including a considerable number of those particularly interested in the medical aspects of the subject. The basic principle of the present-day classification is that of *binomial nomenclature,* first consistently used by Linnæus, in 1751 and expanded by him in the tenth edition of his "Systema Naturæ" (1758).

THE INTERNATIONAL CODE OF ZOOLOGICAL NOMENCLATURE

Linnæus derived his genus and species concepts from Greek logic. In the earlier editions of his work he employed several lines of descriptive text to differentiate species, but in the tenth edition he limited the species description to a single word, in order to save expense in publication. Thus, by a combination of Greek logic and by force of circumstance was binomial nomenclature born.

For nearly a century and a half following Linnæus' time various individuals or groups of individuals attempted to modify or supplement this code, but without marked success In 1889 R. Blanchard presented to the First International Zoölogical Congress in Paris a Code which was adopted by that and the subsequent Congress (1892) but failed to receive universal sanction. At the Third Congress (1895) an international commission was appointed to develop a code which would be acceptable to all groups of zoölogists. Progress reports were made at the Fourth and Fifth Congresses and at the Sixth Congress (1904) the commission was made permanent and a subcommission, which had been previously delegated "to edit the code in English, French and German," presented The International Code of Zoölogical Nomenclature.

This code consists of thirty-six simple articles, supplemented by recommendations and discussion These articles, together with the "Code of Ethics" and "Suspension of Rules in Certain Cases," are as follows:

GENERAL CONSIDERATIONS

"*Article* 1.—Zoölogical nomenclature is independent of botanical nomenclature in the sense that the name of an animal is not to be rejected simply because it is

identical with the name of a plant. If [illegible]

"*Article* 3.—The scientific names of animals must be words which are either Latin or Latinized, or considered and treated as such in case they are not of classic origin.

Family and Subfamily Names

"*Article* 4.—The name of a family is formed by adding the ending *idæ*, the name of a subfamily by adding *inæ*, to the root of the name of its type genus.

"*Article* 5.—The name of a family or subfamily is to be changed when the name of its type genus is changed.

Generic and Subgeneric Names

"*Article* 6.—Generic and subgeneric names are subject to the same rules and recommendations, and from a nomenclatural standpoint they are coördinate, that is, they are of the same value.

"*Article* 7.—A generic name becomes a subgeneric name, when the genus so named becomes a subgenus, and *vice versa*.

"*Article* 8.—A generic name must consist of a single word, simple or compound, written with a capital initial letter, and employed as a substantive in the nominative singular. Examples: *Canis, Perca, Ceratodus, Hymenolepis.*

"*Article* 9.—If a genus is divided into subgenera, the name of the typical subgenus must be the same as the name of the genus (see Article 25).

"*Article* 10.—When it is desired to cite the name of a subgenus, this name is to be placed in parentheses between the generic and the specific names. Examples: *Vanessa (Pyrameis) cardui.*

Specific and Subspecific Names

"*Article* 11.—Specific and subspecific names are subject to the same rules and recommendations, and from a nomenclatural standpoint they are coördinate, that is, they are of the same value.

"*Article* 12.—A specific name becomes a subspecific name when the species so named becomes a subspecies, and *vice versa*.

"*Article* 13.—While specific substantive names derived from names of persons may be written with a capital initial letter, all other specific names are to be written with a small initial letter. Examples: *Rhizostoma Cuvieri* or *Rh. cuvieri*, *Francolinus Lucani* or *F. lucani*, *Hypoderma Diana* or *H. diana*, *Laophonte Mohammed* or *L. mohammed*, *Oestrus ovis*, *Corvus corax.*

"*Article* 14.—Specific names are:

"(*a*) Adjectives, which must agree grammatically with the generic name. Example: *Felis marmorata.*

"(*b*) Substantives in the nominative in apposition with the generic name. Example: *Felis leo.*

"(*c*) Substantives in the genitive. Examples: *rosæ, sturionis, antillarum, galliæ, sancti-pauli, sanctæ-helenæ.*

"If the name is given as a dedication to one or several persons, the genitive is formed in accordance with the rules of Latin declination in case the name was employed and declined in Latin. Examples: *plinii, aristotelis, victoris, antonii, elisabethæ, petri* (given name).

"If the name is a modern patronymic, the genitive is always formed by adding, to the exact and complete name, an *i* if the person is a man, or an *æ* if the person is a woman, even if the name has a Latin form; it is placed in the plural if the dedication involves several persons of the same name. Examples: *cuvieri, möbiusi, nuñezi, merianæ, sarasinorum, bosi* (not *bovis*), *salmoni* (not *salmonis*).

"*Article* 15—The use of compound proper names indicating dedication, or of compound words indicating a comparison with a simple object, does not form an exception to Article 2. In these cases the two words composing the specific name are written as one word with or without the hyphen. Example: *sanctæ-catharinæ* or *sanctæcatharinæ, jan-mayeni* or *janmayeni, cornu-pastoris* or *cornupastoris, coranguinum* or *coranguinum, cedo-nulli* or *cedonulli.*

"Expressions like *rudis planusque* are not admissible as specific names.

"*Article* 16—Geographic names are to be given as substantives in the genitive, or are to be placed in an adjectival form. Examples: *sancti-pauli, sanctæ-helenæ, edwardiensis, diemensis, magellanicus, burdigalensis, vindobonensis.*

"*Article* 17.—If it is desired to cite the subspecific name, such is written immediately following the specific name, without the interposition of any mark of punctuation Example: *Rana esculenta marmorata* Hallowell, but not *Rana esculenta* (*marmorata*) or *Rana marmorata*, Hallowell.

"*Article* 18—The notation of hybrids may be given in several ways; in all cases the name of the male parent precedes that of the female parent, with or without the sexual signs:

"(*a*) The names of the two parents are united by the sign of multiplication (×) Example: *Capra hircus* ♂ × *Ovis aries* ♀ and *Capra hircus* × *Ovis aries* are equally good formulæ

"(*b*) Hybrids may also be cited in form of a fraction, the male parent forming the numerator and the female parent the denominator Example: $\frac{\textit{Capra hircus.}}{\textit{Ovis aries}}$ This second method is in so far preferable that it permits the citation of the person who first published the hybrid form as such. Example: $\frac{\textit{Bernicla canadensis}}{\textit{Anser cygnoides}}$ Rabé.

"(*c*) The fractional form is also preferable in case one of the parents is itself a hybrid. Example: $\frac{\textit{Tetrao tetrix} \times \textit{Tetrao urogallus.}}{\textit{Gallus gallus}}$ In the latter case, however, parentheses may be used. Example (*Tetrao tetrix* × *Tetrao urogallus*) × *Gallus gallus*

"(*d*) When the parents of the hybrid are not known as such (*parents*), the hybrid takes provisionally a specific name, the same as if it were a true species, namely, as if it were not a hybrid; but the generic name is preceded by the sign of multiplication Example × *Coregonus dolosus* Fatio

Formation, Derivation and Orthography of Zoological Names

"*Article* 19.—The original orthography of a name is to be preserved unless an error of transcription, a *lapsus calami*, or a typographical error is evident.

"*Article* 20—In forming names derived from languages in which the Latin alphabet is used, the exact original spelling, including diacritic marks, is to be retained. Examples *Selysius, Lamarckia, Kollikeria, Mülleria, Stålia, Krøyeria, Ibañezia, mobiusi, medići, cžjžeki, spitzbergensis, islandicus, paraguayensis, patagonicus, barbadensis, faröensis.*

Author's Name

"*Article* 21—The author of a scientific name is that person who first publishes the name in connection with an indication, a definition or a description, unless it is clear

from the contents of the publication that some other person is responsible for said name and its indication, definition, or description.

"*Article* 22.—If it is desired to cite the author's name, this should follow the scientific name without interposition of any mark of punctuation; if other citations are desirable (date, *sp. n.*, *emend.*, *sensu stricto*, etc), these follow after the author's name, but are separated from it by a comma or by parentheses Examples: *Primates* Linné, 1758, or *Primates* Linné (1758).

"*Article* 23.—When a species is transferred to another than the original genus or the specific name is combined with any other generic name than that with which it was originally published, the name of the author of the specific name is retained in the notation but placed in parentheses Example *Tænia lata* Linné, 1758, and *Dibothriocephalus latus* (Linné, 1758), *Fasciola hepatica* Linné, 1758, and *Distoma hepaticum* (Linné, 1758).

"If it is desired to cite the author of the new combination, his name follows the parentheses. Example: *Limnatis nilotica* (Savigny, 1820) Moquin-Tandon, 1826

"*Article* 24.—When a species is divided, the restricted species to which the original specific name of the primitive species is attributed may receive a notation indicating both the name of the original author and the name of the reviser. Example. *Tænia solium* Linné *partim*, Goeze.

The Law of Priority[1]

"*Article* 25 —The valid name of a genus or species can be only that name under

"(*b*) That the author has applied the principles of binary nomenclature

"(*c*) *But no generic name nor specific name, published after December* 31, 1930, *shall have any status of availability (hence also of validity) under the Rules, unless and until it is published either*

"1. *with a summary of characters (seu diagnosis, seu definition, seu condensed description) which differentiate or distinguish the genus or the species from other genera or species*,

"2. *or with a definite bibliographic reference to such summary of characters (seu diagnosis, seu definition; seu condensed description). And further*

"3 *in the case of a generic name, with the definite unambiguous designation of the type species (seu genotype, seu autogenotype, seu orthotype)*

Application of the Law of Priority

"*Article* 26 —The tenth edition of Linné's *Systema Naturæ*, 1758, is the work which inaugurated the consistent general application of the binary nomenclature in zoölogy. The date 1758, therefore, is accepted as the starting point of zoölogical nomenclature and of the law of priority.

"*Article* 27.—The law of priority obtains and consequently the oldest available name is retained:

"(*a*) When any part of an animal is named before the animal itself;

"(*b*) When the larva is named before the adult;

"(*c*) When the two sexes of an animal have been considered as distinct species or even as belonging to distinct genera,

"(*d*) When an animal represents a regular succession of dissimilar generations which have been considered as belonging to different species or even to different genera.

[1] Italicized type represents the amendment adopted by the International Zoölogical Congress, which met in Budapest, September 4 to 9, 1927.

"*Article* 28.—A genus formed by the union of two or more genera or subgenera takes the oldest valid generic or subgeneric name of its components. If the names are of the same date, that selected by the first reviser shall stand.

"The same rule obtained when two or more species or subspecies are united to form a single species or subspecies.

"*Article* 29 —If a genus is divided into two or more restricted genera, its valid nam[illegible]

"

for

"

following rules (*a* to *g*), applied in the following order of precedence:

"I. Cases in which the generic type is accepted *solely* upon the basis of the original publication:

"[illegible] finitely [illegible] other

[illegible] a *new* specific name for one of the species, such use shall be construed as "type by original designation."

"(*c*) A genus proposed with a single original species takes that species as its type. (Monotypical genera.)

"(*d*) If a genus, without originally designated (see *a*) or indicated (see *b*) type, contains among its original species one possessing the generic name as its specific or subspecific name, either as valid name or synonym, that species or subspecies becomes *ipso facto* type of the genus. (Type by absolute tautonymy.)

"II Cases in which the generic type is accepted not solely upon basis of original publication.

"(*e*) The following species are excluded in determining the types of genera.

"α Species which were not included under the generic name at the time of its original publication

"β. Species which were *species inquirendæ* from the standpoint of the author of the generic name at the time of its publication

"γ. Species which the author of the genus doubtfully referred to it.

"(*f*) In case a generic name without originally designated type is proposed as substitute for another generic name, with or without type, the type of either, when established, becomes *ipso facto* the type of the other.

"(*g*) If an author, in publishing a genus with more than one valid species, fails to designate (see *a*) or to indicate (see *b*, *d*) its type, any subsequent author may select the type, and such designation is not subject to change (Type by subsequent designation)

"The meaning of the expression 'select the type' is to be rigidly construed. Mention of a species as an illustration or example of a genus does not constitute a selection of a type.

"*Article* 31.—The division of a species into two or more restricted species is subject to the same rules as the division of a genus. But a specific name which undoubtedly rests upon an error of identification cannot be retained for the misdetermined species even if the species in question are afterward placed in different genera. Example: *Tænia pectinata* Goeze, 1782 = *Cittotænia pectinata* (Goeze), but the species erroneously determined by Zeder, 1800, as '*Tænia pectinata* Goeze' = *Andrya rhopalocephala* (Riehm); the latter species does not take the name *Andrya pectinata* (Zeder).

Rejection of Names

"*Article* 32—A generic or a specific name, once published, cannot be rejected, even by its author, because of inappropriateness. Example: Names like *Polyodon*,

Apus, *albus*, etc., when once published, are not to be rejected because of a claim that they indicate characters contradictory to those possessed by the animals in question

"*Article* 33.—A name is not to be rejected because of tautonymy, that is, because the specific or the specific and subspecific names are identical with the generic name. Examples *Trutta trutta*, *Apus apus apus*.

"*Article* 34 —A generic name is to be rejected as a homonym when it has previously been used for some other genus of animals. Example: *Trichina* Owen, 1835, nematode, is rejected as homonym of *Trichina* Meigen, 1830, insect

Code of Ethics

"Without presuming to be the arbiter of points of general ethics, the Commission is persuaded that there is one phase of this subject upon which it is competent to speak, and in reference to this point it suggests to the Congress the adoption of the following resolution·

"*Whereas*—experience has shown that authors, not infrequently, inadvertently publish as new designations of genera or species, names that are preoccupied, *and*

"*Whereas*—experience has also shown that some other authors, discovering the homonymy, have published new names for the later homonyms in question, *be it therefore*

"Resolved—That when it is noticed by any zoologist that the generic or specific name published by any living author as new is in reality a homonym, and therefore unavailable under Articles 34 and 36 of the Rules on Nomenclature, the proper action, from a standpoint of professional etiquette, is for said person to notify said author of the facts of the case, and to give said author ample opportunity to propose a substitute name.

"*Article* 35—A specific name is to be rejected as a homonym when it has previously been used for some other species of the same genus. Example. *Tænia ovilla* Rivolta, 1878 (*n sp*) is rejected as homonym of *T ovilla* Gmelin, 1790.

"When in consequence of the union of two genera, two different animals having the same specific or subspecific name are brought into one genus, the more recent specific or subspecific name is to be rejected as a homonym.

"Specific names of the same origin and meaning shall be considered homonyms if they are distinguished from each other only by the following differences:

"(*a*) The use of *ae*, *oe* and *e*, as *caeruleus*, *coeruleus*, *ceruleus* *ei*, *i* and *y*, as *chiropus*, *cheiropus*. *c* and *k*, as *microdon*, *mikrodon*.

"(*b*) The aspiration or non-aspiration of a consonant, as *oxyryncus*, *oxyrhynchus*.

"(*c*) *The presence or absence of a c before t, as autumnalis, auctumnalis.*

"(*d*) By a single or double consonant, *litoralis*, *littoralis*.

"(*e*) By the ending *ensis* and *iensis* to a geographical name, as *timorensis*, *timoriensis*.

"*Article* 36. Rejected homonyms[1] can never be again used Rejected synonyms can again be used in case of the restoration of erroneously suppressed groups. Example *Tænia Giardi* Moniez, 1879, was suppressed as a synonym of *Tænia ovilla* Rivolta, 1878, later it was discovered that *Tænia ovilla* was preoccupied (*Tænia ovilla* Gmelin, 1790). *Tænia ovilla*, 1878, is suppressed as a homonym and can never again be used, it was still-born and cannot be brought to life, even when the species is placed in another genus (*Thysanosoma*). *Tænia Giardi*, 1879, which was suppressed as a synonym, becomes valid upon the suppression of the homonym *Tænia ovilla* Rivolta

[1] A homonym is defined by Stiles as "one and the same name for two or more different things Synonyms are different names for one and the same thing "

Suspension of Rules in Certain Cases.

"RESOLVED.—That plenary power is herewith conferred upon the International Commission on Zoological Nomenclature, acting for this Congress, to suspend the Règles as applied to any given case, where in its judgement strict application of the

[illegible]

suspension of the Règles as applied to such cases is under consideration, thereby making it possible for zoologists, particularly specialists in the group under question, to present arguments for or against the suspension under consideration; and *provided*, also, that the vote in Commission is unanimously in favor of suspension; and *provided*, further, that if the vote in Commission is a two-thirds majority of the full Commission, but not a unanimous vote in favor of suspension, the Commission is hereby instructed to report the facts to the next succeeding International Congress, *and*

"RESOLVED.—That in the event that a case reaches the Congress, as hereinbefore described, with a two-thirds majority of the Commission in favor of suspension, but without unanimous report, it shall be the duty of the President of the Section on Nomenclature to select a special board of 3 members, consisting of one member of the Commission who voted on each side of the question and one ex-member of the Commission who has not expressed any public opinion on the case, and this special board shall review the evidence presented to it, and its report, either majority or unanimous, shall be final and without appeal, so far as the Congress is concerned, *and*

"RESOLVED.—That the foregoing authority refers in the first instance and especially to cases of names of larval stages and the transference of names from one genus or species to another, *and*

"RESOLVED —That the Congress fully approves the plan that has been inaugurated by the Commission of conferring with special committees from the special group involved in any given case, and that it authorizes and instructs the Commission to continue and extend this policy "

During the 13th International Congress of Zoology held in Paris, July, 1948 the International Commission on Zoological Nomenclature achieved several important advances in zoölogical nomenclature. In a revised text of the "Rules" the decisions hitherto embodied only in the "Opinions" of the Commission are to be incorporated into the "Rules." Special "Schedules" attached to the "Rules" will embo[illegible] particular cases. In the future decisions [illegible] issued as "Declarations," for proposed [illegible] while decisions on individual cases will be issued as "Opinions." Before long all of the body of international law with reference to zoölogical nomenclature will be available in a single volume. It is planned to enlarge the "Official List of Generic Names in Zoölogy" and to issue a companion official list of species, names which are not to be changed for nomenclatorial reasons alone without previous approval of the Commission (Hemming 1948, Science 108, No. 2798, 156–157).

DISCUSSION

While this code is not mandatory on workers in zoölogy and allied sciences, it has been urged in the interests of uniformity. Furthermore, it

has now come to receive almost universal recognition. Unfortunately, the

bewildered by having to recognize old forms under new names. Such real difficulties as these almost always bring about inquiries as to why the names of zoological species, when once established, should require continual revision. In answering the difficulty it may be stated that if the first designation of a species following the year 1758 had been accurate, and if the published description of the species had been sufficiently complete to enable subsequent workers to recognize the species, then under ordinary circumstances t

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related species. Linnæus himself (1758) grouped the beef tapeworm of man (*T. saginata* Goeze, 1782), and the tænia of the dog (*T. hydatigena* Pallas, 1766), together with the pork tapeworm, under the single name *Tænia solium*.

In many instances the accumulation of data through the years has required the division of one genus such as *Distoma* Retzius, 1790, which originally included all of the distomate digenetic flukes, into many genera, so that such species as *Fasciolopsis buski* (Lank., 1857), *Clonorchis sinensis* (Cobbold, 1875), and *Paragonimus westermani* (Kerbert, 1878), which had originally been placed in the genus *Distoma*, were removed by later workers for good and sufficient reasons and placed in more restricted groups. Furthermore, where two or more investigators described the same species at about the same time under different names, it has been necessary to discover which of these names has priority and which is to be regarded as a synonym of the other [Example: *Fasciolopsis buski* (Lank., 1857) has priority over *F. crassum* (Cobbold, 1860), the latter being a synonym.] Again, numerous instances have come to light in which an original description (*post* 1758) has long been buried in the literature and actually had priority over commonly recognized names subsequently given. Fortunately for the medical man such instances in medical zoölogy are not common.

In the case of genera it is not permitted to use the same generic name in more than one group of the Animal Kingdom. Hence the term *Trichina* Owen, 1835, was found by Railliet to be unavailable for the nematode parasite which had commonly been referred to as "*Trichina spiralis*," because it had been previously used for a group of Diptera (1830). In consequence of this fact Railliet (1895) renamed the nematode genus *Trichinella*.

In no small number of cases the larval stage of the worm was known and described before the adult had been discovered. According to the Rules the first name given to any stage of the life cycle of an organism (Article 27*b*) has precedence over a later one, even though that first name was used to designate the larva. Thus *Echinococcus granulosus* (Goeze, 1786) has priority over *Echinococcifer echinococcus* (Zeder, 1803) Weinland, 1858, and *Tænia echinococcus* (Zeder, 1803), whether reference is made to the hydatid

in man, sheep, ox and pig or to the adult tapeworm in the dog. *Strongyloides stercoralis* (Bavay, 1876), first designated for the free-living stage of the Cochin-China worm, also takes precedence over *Strongyloides intestinalis* (Bavay, 1877), the name first applied to the parasitic generation.

In a few instances involving helminths parasitic in man, forms originally believed to be different species of the same genus are now known to be one and the same species. Thus *Clonorchis sinensis* (Cobbold, 1875) and *C. endemicus* (Baelz, 1883) have been united under the name *Clonorchis sinensis*, and *Fasciolopsis buski* (Lank., 1857), *F. rathouisi* (Poirier, 1887), *F. fülleborni* Rodenwaldt, 1909, and *F. goddardi* Ward 1909 are all now referred to as *Fasciolopsis buski.*

Confusion in synonymy has also been due to considering organisms morphologically similar but occurring in different hosts or in the same hosts in different geographical areas as distinct species. A case in point is *Paragonimus westermani* (Kerbert, 1878) from the tiger and *P. ringeri* (Cobbold, 1880) from man. Since the species from man is now usually considered to be identical with that from the tiger, the human parasite is designated by the earlier name. Another case in point is the hookworm of the Tropics and Subtropics, originally described by Gomez de Faria (1910) from the dog and the cat in Rio as *Ancylostoma braziliense* and by Looss (1911) from the civet cat in Ceylon as *A. ceylanicum.* For several years these were believed to be different species but have laterly been considered as identical. There is still doubt as to whether the common ascarid of man and of the pig is one and the same species. Although the worms are morphological the same, the pig has not yet been proved to be a physiologically adapted host for strains of the organism originating from man. On the other hand, experimental evidence is fairly convincing that the dwarf tapeworm of man, *Hymenolepis nana* (v. Siebold, 1852), is identical with *Hymenolepis fraterna* Stiles, 1906, of the rat. In such instances where the human material was first described no serious difficulty arises in nomenclature for one interested only in human helminths, but where the description of the parasites from man does not take precedence over that from other hosts, it is important for the physician to know whether there are prior claims that must be recognized.

Perhaps the greatest difficulty in the whole system of nomenclature and certainly that working the greatest hardship for medical men, is the sudden change of a long-established name for what seems to be a new one. For example, the broad tapeworm commonly referred to as "*Bothriocephalus latus*" or "*Dibothriocephalus latus*" has within recent years been renamed "*Diphyllobothrium latum,*" in view of the fact that the genus *Bothriocephalus* [illegible] intestines of fishes, [illegible] lies, the adults of [illegible] Subsequent removal of the filaria, commonly referred to as "*Filaria bancrofti*" to *Wuchereria* (*i. e.*, *Wuchereria bancrofti*), and the pinworm, "*Oxyuris vermicularis*" to *Enterobius* (*i. e.*, *Enterobius vermicularis*), has been based on different but justifiable grounds, but, to the student not interested in the technical details of nomenclature, such changes may appear to be ill-advised

or at least unnecessary. It is recognized that long continuous usage, particularly of terms commonly employed in medicine, might rightly constitute a sufficient reason for setting aside the strict application of the rules of nomenclature, but, on the other hand, if exceptions are made in one series of cases, it is altogether likely that other types of exceptions might be asked for on equally plausible grounds. (See "Suspension of Rules in Certain Cases" under Art. 36, above.)

Only one name applied to a helminth parasite of man has given rise to real orthographic difficulties. That name is the one used for the hookworm originally described by Dubini (1843) as *Agchylostoma duodenale*. In view of the fact that the first two syllables of the generic name as given by Dubini were barbarian rather than classical in their origin, the International Commission on Zoölogical Nomenclature adopted *Ancylostoma* as the correct form. Such variants as *Anchylostoma*, *Ankylostoma* and *Ankylostomum* are therefore not considered proper usage. As a matter of consistency the term designating an infection with hookworm of the genus *Ancylostoma* should be ancylostomiasis and not anchylostomiasis or ankylostomiasis. (Uncinariasis, which is commonly employed to designate infection with *Necator americanus*, should be reserved for infections with *Uncinaria*, a genus of hookworms occurring in the dog, cat, fox, pig and badger.) In this connection the term "*Bilharzia*", which is commonly used for the blood-fluke infections, *Schistosoma hæmatobium* and *S. mansoni*, is an absolute synonym of the term *Schistosoma*, and should never be used in a nomenclatural sense.

Enough has been said by way of comment to show that the Code of Zoölogical Nomenclature, although necessarily arbitrary, is entirely consistent, and that difficulties which have arisen have usually resulted from inherent errors in designations made by various authors or by their incorrect application of the Rules. One extraordinary difficulty, that of "physiological species," cannot be solved by the Code, which is by its very nature a static instrument.

OFFICIAL GENERIC NAMES OF PARASITIC HELMINTHS OF MAN, BASED ON OPINIONS RENDERED BY THE INTERNATIONAL COMMISSION ON ZOÖLOGICAL NOMENCLATURE

Opinion 66 (Feb., 1915). NEMATHELMINTHES. *Ancylostoma*, type *duodenale*, *Ascaris*, type *lumbricoides*, *Dracunculus*, type *medinensis*, *Gnathostoma*, type *spinigerum*; *Necator*, type *americanus*; *Strongyloides*, type *stercoralis*. *Trichostrongylus*, type *retortæformis*, *Gordius*, type *aquaticus*, *Paragordius*, type *varius*.

Opinion 77 (Jan. 31, 1922). TREMATODA.—*Schistosoma*, type *hæmatobium*. CESTODA.—*Hymenolepis*, type *diminuta*.

Opinion 84 (Dec. 16, 1925). TREMATODA.—*Dicrocælium*, type *lanceatum* (vel *dendriticum* sub judice); *Fasciola*, type *hepatica*, *Heterophyes*, type *heterophyes*. CESTODA.—*Davainea*, type *proglottina*, *Dipylidium*, type *caninum*, *Echinococcus*, type *granulosus*, *Tænia*, type *solium*.

Opinion 104 (Sept. 19, 1928). CESTODA. *Ligula*, type *avium*. NEMATODA.—*Heterodera*, type *schachtii*, *Rhabditis*, type *terricola*, *Syngamus* type *trachea*.

OPINIONS OF THE AMERICAN SOCIETY OF PARASITOLOGISTS

Report of the Committee on Terminology (December, 1934)[1]

The Committee stated that its functions were "informative and advisory and that any attempts at legislation are unwarranted."

Infection vs. Infestation.—The terms *infect* and *infection* are "properly applicable wherever the parasite invades and establishes itself within the body of the host, including, in this sense, the gastro-intestinal tract. This would apply then, not only to bacteria and protozoa, but also the helminths and those insects, such as the bot and warble flies, which become internal parasites" . . . "We believe that *infest* and *infestation* ought to revert to their original use in connection with external, and in most cases visible, agents" . . . "We fail to see any reason for continuing the use of the term infestation as applied to internal parasites and believe that the present confusion will disappear only if its use be discontinued."

Host-Specificity, etc.—"There may be *host-specificity* on the part of a given parasite, but it can hardly be maintained that the converse exists, namely *parasite-specificity* on the part of a given host."

Symbiosis, Symbiont and Symbiote.—According to de Bary (1879), who first employed the term, *symbiosis* is a general term "characterizing the living together of unlike organisms," including all degrees of parasitism, commensalism and mutualism. "The terms *symbiont* and *symbiote* are applied to the members of the symbiotic relationship and may properly be used for either member, though it has become the custom to refer to the smaller as the *symbiont* or *symbiote* and to the larger as the *host.*"

Report of the Committee on Nomenclature (December, 1940)[2]

"It was the opinion of the Committee that under the International Rules of Zoological Nomenclature *Trichuris* rather than *Trichocephalus* is the valid generic name, and that *Dioctophyma renale* is the valid name for the giant kidney worm."

NAMES OF PARASITIC HELMINTHS OF MAN AND PATHOLOGICAL DESIGNATIONS FOR INFECTIONS WITH THESE PARASITES

Name of Parasite	Pathological Designation for Infection with this Parasite[3]
PLATYHELMINTHES	
TREMATODA	trematodiasis or fluke infection
Centrocestus armatus (Tanabe, 1922)	
Centrocestus formosanus (Nishigori, 1924)	
**Clonorchis sinensis* (Cobbold, 1875)	clonorchiasis or Chinese liver-fluke infection
Dicrocœlium dendriticum Rud., 1819	dicrocœliasis or *Dicrocœlium* infection

[1]Reference Jour Parasitol, **23**, 325–329, 1937

[2]Reference Jour Parasitol, **27**, 277, 279–282, 1941.

* Common helminth infections of man

Name of Parasite	Pathological Designation for Infection with this Parasite[1]
Diorchitrema pseudocirratum Witenberg, 1929	
Echinochasmus perfoliatus (v. Rátz, 1908)	
Echinoparyphium paraulum (Dietz, 1909)	
Echinoparyphium recurvatum (v. Linstow, 1873)	
Echinostoma cinetorchis Ando and Ozaki, 1923	
Echinostoma ilocanum Garrison, 1908	
Echinostoma melis (Schrank, 1788) Dietz, 1909 syn. *E. jassyense* (Leon and Ciurea, 1922)	
Echinostoma lindoënse Sandground and Bonne, 1940	
Echinostoma macrorchis Ando and Ozaki, 1923	
Echinostoma malayanum Leiper, 1911	
Echinostoma revolutum (Fröhlich, 1802)	
Eurytrema pancreaticum (Janson, 1889)	
Fasciola gigantica Cobbold, 1855	
Fasciola hepatica Linnæus, 1758	fascioliasis hepatica or sheep liver-fluke infection
**Fasciolopsis buski* (Lankester, 1857)	fasciolopsiasis or giant intestinal fluke infection
Gastrodiscoides hominis (Lewis and McConnell, 1876)	*Gastrodiscoides* infection
Haplorchis microrchia (Katsuta, 1932)	
[illegible]	
[illegible]	
*[illegible]	*Heterophyes* infection
[illegible]	*Heterophyes* infection
[illegible]	
Metagonimus minutus Katsuta, 1932	
Metagonimus yokogawai Katsurada, 1912	*Metagonimus* infection
**Opisthorchis felineus* (Rivolta, 1884)	opisthorchiasis
Opisthorchis noverca Braun, 1902	
Opisthorchis viverrini (Poirier, 1886)	
**Paragonimus westermani* (Kerbert, 1878)	paragonimiasis or pulmonary distomiasis
[illegible] 15)	
[illegible] 41	
[illegible] 1911	
[illegible]	
[illegible]	schistosomiasis bovis
**Schistosoma hæmatobium* (Bilharz, 1852)	schistosomiasis hæmatobia vesical or urinary schistosomiasis
**Schistosoma japonicum* Katsurada, 1904	schistosomiasis japonica

[1] Formed by the addition of "iasis," or at times of "osis," to the root of the genus name and requiring agreement of the species name in case the latter is an adjective. For the rarer infections the technical pathological designation is seldom used, and is consequently omitted here. *Pathological terms are not capitalized.*

† Accidental or pseudo-parasites.

* Common helminth infections of man.

Name of Parasite	Pathological Designation for Infection with this Parasite[1]
**Schistosoma mansoni* Sambon, 1907	schistosomiasis mansoni, Manson's schistosomiasis
Schistosoma spindale Mongomery, 1906	
Stellantchasmus amplicaecalis Katsuta, 1932	
Stellantchasmus falcatus Onji and Nishio, 1916	
Stellantchasmus formosanus Katsuta, 1932	
Troglotrema salmincola (Chapin, 1926)	
Watsonius watsoni (Conyngham, 1904)	
CESTOIDEA	cestodiasis or tapeworm infection
Bertiella studeri (Blanchard, 1891)	
Braunia jassyensis Léon, 1908	
Digramma brauni (Léon, 1907)	
Diphyllobothrium cordatum (Leuckart, 1863)	
Diphyllobothrium houghtoni Faust, Campbell and Kellogg, 1929	
**Diphyllobothrium latum* (Linn., 1758)	broad fish tapeworm infection
Diplogonoporus grandis (Blanchard, 1894)	
Dipylidium caninum (Linn., 1758)	
Drepanidotænia lanceolata (Bloch, 1782)	
**Echinococcus granulosus* (Batsch, 1786)	hydatid cyst, *Echinococcus* disease, echinococciasis or echinococcosis
Hymenolepis diminuta (Rud., 1819)	hymenolepiasis diminuta or rat tapeworm infection
**Hymenolepis nana* (v. Siebold, 1852)	hymenolepiasis nana or dwarf tapeworm infection
Inermicapsifer cubensis (Kouri, 1939)	
Ligula intestinalis (Goeze, 1782)	
Mesocestoides variabilis Mueller, 1928	
Multiceps glomeratus Rail. and Henry, 1915	
Multiceps multiceps (Leske, 1780)	
Multiceps serialis (Gervais, 1845)	
Raillietina asiatica (v. Linstow, 1901)	
Raillietina celebensis Janicki, 1902	
Raillietina garrisoni Tubangui, 1931	
Raillietina madagascariensis (Davaine, 1869)	
Raillietina quitensis L. A. Léon, 1935	
Sparganum baxteri Sambon, 1907	
**Sparganum mansoni* (Cobbold, 1882)	sparganiasis or spargonosis
Sparganum mansonoides (Mueller, 1935)	
Sparganum proliferum (Ijima, 1905)	
Tænia africana v. Linstow, 1900	
Tænia confusa Ward, 1896	
**Tænia saginata* Goeze, 1782	tæniasis saginata or beef tapeworm infection

[1] Formed by the addition of "iasis," or at times of "osis," to the root of the genus name and requiring agreement of the species name in case the latter is an adjective. For the rarer infections the technical pathological designation is seldom used, and is consequently omitted here. *Pathological terms are not capitalized.*

* Common helminth infections of man.

Name of Parasite	Pathological Designation for Infection with this Parasite[1]
*_Tænia solium_ Linn., 1758	tæniasis solium or pork tapeworm infection
Tænia tæniæformis (Batsch, 1786)	
NEMATODA	nematodiasis or roundworm infection
*_Acanthocheilonema perstans_ (Manson, 1891)	_Acanthocheilonema_ infection
Acanthocheilonema streptocerca (Macfie and Corson, 1922)	
†_Agamomermis_ spp.	
*_Ancylostoma braziliense_ de Faria, 1910	
*_Ancylostoma duodenale_ (Dubini, 1843)	ancylostomiasis
Ancylostoma malayanum (Alessandrini, 1905)	
*_Ascaris lumbricoides_ Linn., 1758	ascariasis or large roundworm infection
Capillaria hepatica (Bancroft, 1893)	
Dioctophyma renale (Goeze, 1782)	
Dirofilaria louisianensis Faust, Thomas and Jones, 1941	
Dirofilaria magalhãesi (Blanchard, 1896)	
Dirofilaria repens Railliet and Henry, 1911	
*_Dracunculus medinensis_ (Linn., 1758)	dracunculosis or dracontiasis, Medina worm infection
*_Enterobius vermicularis_ (Linn., 1758)	enterobiasis, oxyuriasis, pinworm or seatworm infection
Gnathostoma hispidum Fedtsch., 1872	
Gnathostoma spinigerum Owen, 1836	
Gongylonema pulchrum Molin, 1857	
Hæmonchus contortus (Rud., 1803)	
†_Heterodera marioni_ (Cornu, 1879)	
Lagochilascaris minor (Leiper, 1909)	
*_Loa loa_ (Cobbold, 1864)	loaiasis or _Loa_ infection
Mansonella ozzardi (Manson, 1897)	
Mecistocirrus digitatus (v. Linstow, 1906)	
Metastrongylus elongatus (Dujardin, 1845)	
*_Necator americanus_ (Stiles, 1902)	necatoriasis or "uncinariasis"
Oesophagostomum apiostomum (Willach, 1891)	
Oesophagostomum stephanostomum, var. _thomasi_ Rail. and Henry, 1909	
*_Onchocerca volvulus_ (Leuckart, 1893)	onchocerciasis or onchocercosis
Ostertagia ostertagi (Stiles, 1892)	
Physaloptera caucasica v. Linst., 1902	
†_Rhabditis hominis_ Kobayashi, 1914	
†_Rhabditis niellyi_ (Blanchard, 1885)	
†_Rhabditis pellio_ (Schneider, 1866)	

[1] Formed by the addition of "iasis" or at times of "osis" to the root of the genus name and requiring agreement of the species name in case the latter is an adjective. For the rarer infections the technical pathological designation is seldom used, and is consequently omitted here. _Pathological terms are not capitalized._

† Accidental or pseudo-parasites.

* Common helminth infections of man.

Name of Parasite	Pathological Designation for Infection with this Parasite[1]
**Strongyloides stercoralis* (Bavay, 1876)	strongyloidiasis or strongyloidosis
Syngamus laryngeus Railliet, 1899	
Syphacia obvelata (Rud., 1802)	
Ternidens deminutus (Rail. and Henry, 1905)	
Thelazia californiensis Kofoid and Williams, 1935	
Thelazia callipæda Rail. and Henry, 1910	
Toxocara canis (Werner, 1782)	
Toxocara cati (Schrank, 1788)	
**Trichinella spiralis* (Owen, 1835)	trichinelliasis or trichinosis
**Trichocephalus trichiurus* (Linn., 1771)	trichocephaliasis or trichuriasis
Trichostrongylus axei (Cobbold, 1879)	
Trichostrongylus colubriformis (Giles, 1892)	
[illegible]	
Trichostrongylus vitrinus Looss, 1905	
†*Turbatrix aceti* (Mueller, 1783)	
†*Tylenchus dipsaci* Gervais and van Beneden, 1859	
**Wuchereria bancrofti* (Cobbold, 1877)	filariasis bancrofti or Bancroft's filariasis
Wuchereria malayi (Brug, 1927)	malayan filariasis
ACANTHOCEPHALA	acanthocephaliasis
Macracanthorhynchus hirudinaceus (Pallas, 1781)	
Moniliformis moniliformis (Bremser, 1819)	
HIRUDINEA	hirudiniasis or leech infestation
Limnatis nilotica	internal hirudiniasis
Hæmadipsa spp., *et al*	external hirudiniasis

[1] Formed by the addition of "iasis," or at times of "osis," to the root of the genus name and requiring agreement of the species name in case the latter is an adjective For the rarer infections the technical pathological designation is seldom used, and is consequently omitted here *Pathological terms are not capitalizeed.*

*Common helminth infections of man

†Accidental or pseudo-parasites

SECTION II

THE PLATYHELMINTHES OR FLATWORMS

CHAPTER VIII

THE FLATWORMS AS A GROUP

GENERAL CONSIDERATIONS

LINNÆUS (1758) and biologists of his day referred to all metazoan organisms which were more or less worm-like at one time or another of their life cycle as **Vermes** or "worms." More strictly speaking, the term "Vermes" has come to be utilized as a group name for all flatworms, roundworms and annelids or segmented worms, each of which group constitutes a distinct phylum of the **Animal Kingdom**. Of these three phyla, the most simple in organization and that nearest the archetype of the bilaterally symmetrical Metazoa is the group of the flatworms or **Platyhelminthes**.

The **Platyhelminthes** comprise all of those species of worms which are bilaterally symmetrical and which are usually compressed dorso-ventrally. There is no body cavity in the definitive stage of the organism, the space being filled with spongy undifferentiated parenchymatous cells. The nervous system consists of paired ganglia with transverse commissures near the anterior end of the worm, constituting the central coördinating nerve center or "brain," and longitudinal nerve trunks arising from the "brain," proceeding both anteriorwards and posteriorwards, with terminal nerve endings. Some members of this phylum are characterized by having a single gastric cavity, which, if present, ordinarily terminates blindly without an anus. All flatworms possess a bilaterally symmetrical excretory system, consisting of a bladder (or primitively twinned bladders), collecting tubules, capillaries and terminal "flame-cells" or *solenocytes*. The "flame-cells" are so designated because they, as the terminal cells of the capillaries, are each provided with a group of vibratile cilia, which lie within the enlarged termini of the capillaries and beat in unison so as to give the appearance of a flickering candle flame. In the absence of a circulatory system (except in the group of the nemerteans) the excretory system cares for the elimination of all liquid and gaseous wastes from the intimate tissues of the body.

The sexual organs of the **Platyhelminthes** call for special consideration. They are complicated and consist of both primary and secondary organs of both sexes. Usually both sexes are combined in a single organism, which is consequently hermaphroditic. Each organism is thus self-sufficient in the production of fertilized eggs. In the majority of the tapeworms the body is "segmented" and each "segment" (*i. e.*, proglottid) carries a complete set of male and female reproductive organs. In a few genera (*Dipylidium*, *Diplopylidium*, *Diplogonoporus*) there is a double set of reproductive organs in each proglottid. In addition to bisexual propaga-

tion, other methods of reproduction may be intercalated, as, for example, budding in the Turbellaria and cestodes, and parthenogenesis or other sexual processes in the trematodes.

Development may be direct, as in the case of certain Turbellaria and ectoparasitic trematodes; or it may require a larval stage with incomplete metamorphosis, as in the Aspidogastrea, or with more complete metamorphosis, as in the cestodes; or it may consist in an alternation (*metagenesis*) of three or more distinct generations, as in the endoparasitic trematodes.

The phylum **Platyhelminthes** is usually divided into four classes, the Turbellaria, the Trematoda, the Cestoidea and the Nemertea. The last-named group consists almost exclusively of free-living forms, possessing, in addition to a circulatory system, a conspicuous proboscis and an anus. The relationship of this class to the other members of the phylum is still questionable. Some zoologists believe that the Temnocephalida constitute an intermediate group between the Turbellaria and the Trematoda, while others, including Hyman (1947), consider them to be rhabdocele turbellarians.

CLASSIFICATION OF THE FLATWORMS

Phylum **Platyhelminthes** Gegenbauer, 1859.

Many-celled invertebrate animals, usually leaf- or tape-like, rarely cylindrical; bilaterally symmetrical; with three embryological layers; alimentary canal, when present, single, ordinarily without an anal opening; without a body cavity, excretory system provided with flame-cells (*solenocytes*); primitively with ciliated ectodermal covering.

Class I.—Turbellaria Ehrenberg, 1831.

Mostly free-living organisms, only a few species being commensals or parasites; body covered with cilia; with or without a sucker; circulatory system lacking; development usually direct, without metamorphosis; reproduction hermaphroditic.

Class II —Trematoda Rudolphi, 1808.

Exclusively parasitic organisms; adults covered with a non-ciliated integument, ciliated epithelium confined to larvæ (*miracidia*) hatched from eggs; suckers almost always present; circulatory system lacking; alimentary canal present except in the sporocyst generation of the Digenea.

Class III.—Cestoidea (Rudolphi, 1808) Fuhrmann, 1931.

Exclusively parasitic organisms; adults hermaphroditic, covered with a non-ciliated integument; ciliated epithelium when present confined to embryos hatched from eggs; scolex provided with suckers and frequently with hooklets; circulatory system lacking; no alimentary canal, body (*strobila*) in almost all species divided transversely into "segments" (*i. e., proglottids*).

Class IV.—Nemertea von Siebold and Stannius, 1842.

Almost exclusively free-living organisms; body covered with cilia; with a proboscis and an anus; circulatory system present; animals mostly unisexual (*i. e.*, diecious); reproduction direct or with a larval stage.

Since only the trematodes and cestodes are parasitic in man, attention will be directed in the following pages to these two groups.

The relationship and theoretically common origin of these four Class groups of the Phylum **Platyhelminthes** are schematically represented in Fig. 1.

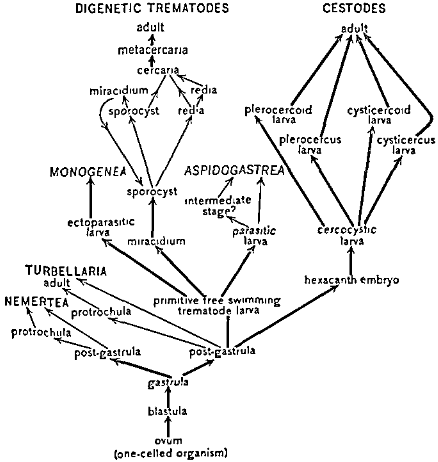

FIG. 1. Synoptic diagram of the origin and relationship of the Platyhelminthes

CHAPTER IX

THE TREMATODES OR FLUKES. STRUCTURE AND LIFE HISTORY

GENERAL CONSIDERATIONS

The trematodes or flukes are **Platyhelminthes** which are true parasites during a very large portion of their entire life. They derive their name from the fact that they are usually provided with conspicuous suckers (*e. g.*, are "pierced with holes," from the Greek, *τρηματώδης*). There is almost a complete series of forms, represented, on the one hand, by those species which are wholly ectoparasitic on aquatic hosts and, on the other, by those species which have come to reside in the portal blood stream of vertebrates and are most intimately dependent on the particular host in which they live for their existence. Intermediate in the intimacy of their parasitic relationship are various species attached to the gills, buccal cavity, urinary bladder or intestine of their host. Species which have attained only a superficial or ectoparasitic state of parasitism have a relatively simple life cycle, without alternation of generations; they are known as the **Monogenea**, or monogenetic forms. The **Aspidogastrea** also belong to this category. On the other hand, species which have developed a more intimate type of internal parasitism have become involved in a complicated life cycle, with alteration of generations; they are known as the **Digenea**, or digenetic trematodes. All of the species parasitic in man belong to the digenetic trematodes.

STRUCTURE OF THE ADULT TREMATODE

The adult trematode is usually visible to the naked eye. It probably lacks a true epidermis and is covered with a protective integument, the *cuticula*, which is usually provided with scales or spines and is secreted by the under-lying layer of cells, the *hypodermis*. Beneath the hypodermis there are a *transverse muscle layer*, a *longitudinal muscle layer* and *oblique muscles*, while essentially undifferentiated parenchyma cells provide a loose matrix

around the oral openings, and in most species there is at least one secondary sucker or acetabulum on the ventral surface of the fluke. In some instances this secondary acetabulum is much more conspicuous than the oral sucker

In the majority of species the *oral sucker* is situated at or near the anterior end of the body, however, in one group, the Gasterostomata, the oral opening with its sucker is mid-ventral in position near the equatorial plane. Within the oral sucker there is a *pharynx* (muscular in most species) which, in turn, usually leads into an *esophagus*. The esophagus bifurcates anterior to the middle of the body to form a pair of *ceca*. These latter, after bending outwards, proceed posteriorwards to the subdistal region of the worm, where they end blindly. Exceptions are found in a few genera, as

for example *Balfouria*, which possess an anal opening. The ceca may be simple (*Clonorchis*) or branched (*Fasciola*). They may even unite behind the middle of the body to form a single median stem (*Schistosoma*).

The *nervous system* in the digenetic trematode (Fig. 3) consists of paired ganglion cells with a saddle-like series of commissures dorsal to the pharynx and three main nerve trunks on either side, the dorsal, lateral and ventral trunks, extending anteriorward on the one hand and posteriorward on the other. Around the anterior end of the body there are numerous sensory nerve endings and in some groups, particularly in the larval stages, "eye-spots" are present. Melanoid pigment may be found in the tissues superficial to the nervous system during the larval stages.

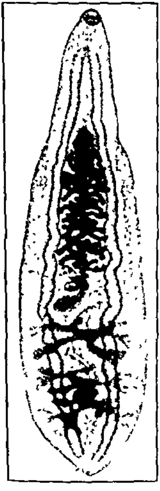

Fig 2

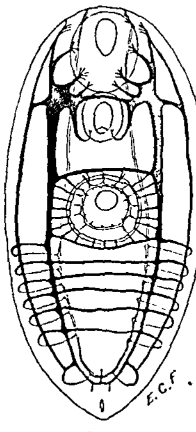

Fig 3

Fig. 2.—Mature *Clonorchis sinensis*, showing digestive, excretory and reproductive organs (For an explanation of the organs in this trematode, *vide* fig. 100, p 212) (Original photograph)

Fig. 3.—Nervous system of a digenetic trematode, showing the three pairs of longitudinal nerve trunks, numerous transverse commissures, and nerve endings for the oral sucker pharynx and ventral acetabulum (Adapted from Bettendorf)

The *excretory system* (Fig. 4) consists of a median, posteriorly disposed *bladder*, which opens through an *excretory pore* guarded by a sphincter.

On its anterior aspect, usually anteriolaterally, the bladder receives a pair of *collecting tubes*, which, upon being traced forward, will be found to branch in a precise manner. This branching may occur once or even several times, until the ultimate *capillaries* are reached, each one ending in a "flame-cell" or *solenocyte*, which is analogous and possibly homologous to the protonephridium of the vertebrate body. The pattern of the excretory system is an exact one; it is always the same for the same species of fluke; it is always reducible to a "least common denominator;" it differs in different families but is usually the same in closely related species. It is, therefore, an important structure in determining the relationship of species and of larvae with adults. Thus the miracidium of most flukes (Fig. 7) has a single flame-cell on each side of its body; that of the blood flukes (Fig. 23) has two such flame-cells; and that of the Aspidogastrea has three. The fundamental flame-cell pattern of a given trematode species can most readily be studied in the cercarial stage, where the system is not ordinarily masked by opaque tissues or cell inclusions. In the cercaria of the human blood flukes there are one anterior and one posterior pair of flame-cells on each side of the body. As the cercaria develops into the adult trematode the flame-cells multiply many times by a dichotomous division, so that the total number of such cells in *the adult is an exact multiple of those in* the cercaria. Thus, the fundamental flame-cell pattern for the human blood flukes may be expressed as: $2[(1 + 1) + (1 + 1)]$ or $2[\alpha + \beta]$, where the figure "2" represents the bilateral condition, "α" the anterior and "β" the posterior group of cells.

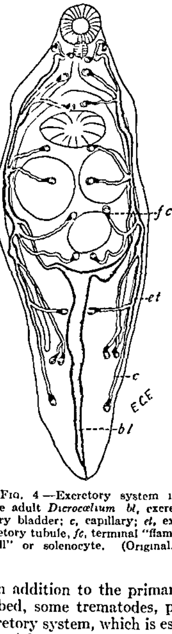

FIG. 4—Excretory system in the adult *Dicrocœlium bl*, excretory bladder; *c*, capillary; *et*, excretory tubule, *fc*, terminal "flame cell" or solenocyte. (Original.)

In addition to the primary excretory system which has just been described, some trematodes, particularly the strigeoids, have an accessory excretory system, which is especially prominent during the encysted metacercarial stage.

A *lymph* or *vascular system*, consisting of two or four main longitudinal trunks and multiple ramifications, has been described for several groups of monostomes and amphistomes (Looss, 1902, 1912; Stunkard, 1929, Willey, 1930). This system apparently develops (during the encysted meta-

cercarial stage of these trematodes) from the fusion of previously separate spaces in the mesenchyma. The rami and trunks transport nutriment from the intestinal ceca throughout the body, but especially to the organs of high metabolic activity, as the ovaries and testes Students of this system regard it as having considerable phylogenetic significance

The most conspicuous and most complicated organs of the adult trematode are the generative or *reproductive organs*. All species of human trematodes except the blood flukes are hermaphroditic. Originally there was reciprocal copulation and many of the species still have provision for this process, but the great majority of the forms which have been studied depend on self-fertilization. The process can be better understood after the generative organs have been described

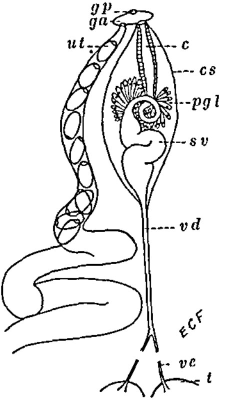

Fig. 5

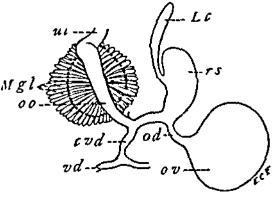

Fig 6

Fig 5.—Male and female reproductive organs of a digenetic trematode in the region of the genital pore. *c*, cirrus organ, *cs*, cirrus sac, *ga*, genital atrium, *gp*, genital pore; *pgl*, prostate glands, *sv*, seminal vesicle, *t*, testis; *ut*, outer uterine tube (*metraterm*), with eggs, *vd*, vas deferens, *ve*, vas efferens (Original)

Fig 6.—Female reproductive organs of a digenetic trematode *cvd*, common vitelline duct, *Lc*, Laurer's canal, *Mgl*, Mehlis' gland, *od*, oviduct, *oo*, oötype, *ov*, ovary, *rs*, seminal receptacle, *ut*, uterus; *vd*, vitelline duct. (Original)

The *male reproductive organs* consist of the following elements (Fig 5). The *testes*, typically two, are usually situated near the ovary. They may lie in the same transverse plane or be situated obliquely to each other or in tandem arrangement. They may be rounded, lobed or dendritic in contour. From each testis (Fig. 5, *t*) there arises a *vas efferens* (*ve*) which is sooner or later joined by its mate to form the *vas deferens* (*vd*), which proceeds towards the genital atrium, enlarging before it reaches the genital atrium into a *seminal vesicle* (*sv*). This may be a simple enlargement of the duct or it may be retort-shaped or even tightly twisted upon itself. Anterior to the seminal vesicle there is usually a cluster of *prostate glands* (*pgl*), and

frequently there is a muscular *cirrus organ* (*c*) just within the genital atrium. The seminal vesicle, prostate glands and cirrus organ, if present, are usually enclosed in an enveloping *cirrus sac* (*cs*). In the case of multiple testes (*e. g., Schistosoma*) there is a vas efferens for each testis. The *spermatozoa* which are produced by the testes pass up the ducts to the seminal vesicle where they are temporarily stored. They then pass out into the genital atrium (*ga*), thence up the uterus, proceeding through the ootype to the seminal receptacle, which constitutes the sperm reservoir of the female system. In a few species there is no seminal receptacle.

The *female reproductive organs* (Fig. 6) consist of a single *ovary* (*ov*) in which the eggs develop, with its duct, the *oviduct*, through which the eggs when mature pass into the *oötype* (*oo*) or chamber where the naked ovum is usually transformed into the fertilized encapsulated egg. The ovary is frequently rounded but may be lobed or dendritic. On its way to the ootype the oviduct receives a common vitelline duct (*cvd*), which arises from the junction of a right and a left vitelline duct, each conveying the products to the common duct from the *vitellaria*, which are usually situated in the extra-cecal fields and consist of clusters of glandular cells with yellowish refractive contents. Previous to receiving the common vitelline duct the oviduct has been joined by the *seminal receptacle* (*rs*) with a dorsal outpocketing, *Laurer's canal* (*Lc*). This canal typically opens to the dorsal surface and is believed to represent a vestigial *vagina* through which originally insemination from another worm of the same species took place. In a number of species Laurer's canal is lacking and in many species it ends blindly without extending to the dorsal surface. In such cases spermatozoa reach the seminal receptacle only after migration up the uterus against the outward current of mature and maturing eggs. The oötype is surrounded by a cluster of acinus glands, known as *Mehlis' gland* (*Mgl*) which are commonly referred to as "shell glands," but which Kouri and Nauss (1938), in a histological study of this structure in *Fasciola hepatica*, have found to bear a striking resemblance to the prostate glands. These workers suggest that the secretions of Mehlis' gland are possibly lubricative in their function. *Stephenson (1947) tent*[illegible] possible hypothesis. Originating from the side of [illegible] *rus* (*ut*), which, after a more or l[illegible] non *genital atrium* (Fig. 5, *ga*), which opens to the outside through the *genital pore* (*gp*). The terminal portion of the uterus is frequently referred to as the *metraterm*.

The process of egg-making, which occurs in the ootype, or in the proximal segment of the uterus, normally proceeds in the living mature worm with regularity and precision. The mature ovum emerges from the ovary, passes into the oötype, and is fertilized by one of several spermatozoa that have either come in from the uterus or from the seminal receptacle. Meanwhile the yolk cells are added and the egg-shell is secreted. In a critical study of egg-shell formation in *Fasciola hepatica* Stephenson (1947) has demonstrated that the egg-shell of this species is derived from basophilic globules or granules containing orthodihydroxyphenol and protein which are present in the vitelline cells. These cells pass through the oötype and *via* a non-return valve into the proximal portion of the uterus Here the

shell-forming material is set free, the vitelline cells, rich in glycogen, become arranged around the ovum, fertilization occurs and the fused vitelline granules form the enveloping shell. The assembled egg is then forced forwards in the uterus and another ovum comes into the ootype. The process is accomplished with the exact coördination of a complicated mechanism, each part of which operates with rhythm and speed synchronized to the whole. The eggs in the proximal end of the uterus are necessarily the youngest, while those in the distal portion are the most mature. The eggs at the time of oviposition have a shell composed of a quinone-tanned protein similar to the sclerotin of the cockroach ootheca. On reaching the outermost portion of the uterus the eggs are passed through the genital atrium and out of the genital pore into the surrounding medium in which the worm lives. In order to proceed with development they must reach the outside world in the hosts' excreta.

THE LIFE CYCLE OF DIGENETIC TREMATODES

The digenetic trematodes not only have an alternation of generations (*metagenesis*) but also an alternation of hosts. The host of the generation producing fertilized eggs is usually a vertebrate; the intermediate host is always a mollusc. In addition, there is a required second intermediate host for many species of flukes. This host is frequently an arthropod or a lower vertebrate. The stage of the life cycle within the mollusc has at times been referred to as asexual, at other times sexual, either as a result of parthenogenesis or of polyembryony. The life cycle of this group therefore involves a definitive, egg-laying stage and two or more alternate generations. Evidence favors the view that the generations which develop in the mollusc are the older, that the mollusc was the original host, and that infection of the vertebrate host is a later adaptation. On the one hand, the uniformity of method utilized by the fluke in infecting the snail and of development within the snail, together with the relative equilibrium of molluscan host and trematode parasite, and, on the other, the variety of ways by which the fluke enters its definite host, the variety of tissues which it parasitizes and the relative dysfunction which it causes in the tissues of the host-all support this view.

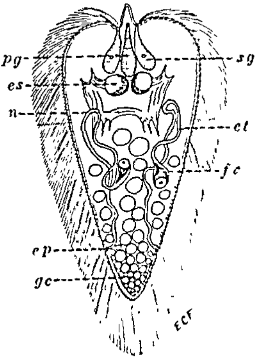

FIG. 7.—Miracidium of *Fasciolopsis buski* showing ciliated epithelium (*ep*), secretory or penetration gland (*sg*), primitive gut (*pg*), excretory system with flame cells (*fc*), excretory tubule (*et*), and excretory pore (*ep*), nerve center (*n*), eyespots (*es*) and proliferating germ cells (*gc*). (Original.)

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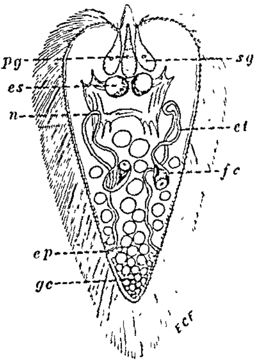


[illegible] flame [illegible] system [illegible] and with flame [illegible] excretory pore (*ep*), nerve center (*n*), eye-spots (*es*) and proliferating germ cells (*gc*). (Original.)

In order for the fertilized egg produced by the trematode in the body of the definitive host to proceed with its development it must reach the outside world. Most flukes live in the intestinal tract of the definitive host or its adnexa. The eggs of those species parasitic in the bile passages reach the intestine through the common duct; the eggs of the lung flukes may be coughed up and either discharged in sputum or swallowed and voided in the feces. The eggs of *Schistosoma japonicum* and *S. mansoni* are expelled from the mesenteric capillaries through the intestinal wall into the intestinal lumen. Thus, all of these eggs normally escape with the feces. On the other hand, the eggs of *Schistosoma hæmatobium* ordinarily escape from the vesical capillaries through the bladder wall into the urinary bladder, and are discharged in the urine.

Some of the eggs, when laid, or at least when discharged in the host's excreta, already contain fully-formed, mature larvæ, as, for example, those of the blood flukes, *Clonorchis, Dicrocœlium* and *Metagonimus*. On the other hand, the eggs of *Fasciolopsis* and *Paragonimus* require a period of incubation after leaving the body of the definitive host before they are mature. The mature egg, when placed in an isotonic or slightly hypotonic medium, such as canal or pond water where feces may be deposited, usually responds by the energetic movement of the larva within, which soon causes the shell to open, either by the "popping off" of the operculum, if such be present, or by a splitting of the shell in non-operculate species. The larva now escapes into the free-water medium and for a brief period is a free-living organism.

The larva which escapes from the egg shell is the *miracidium* (μειράχιον, meaning "little boy"). It is a moderately complicated organism (Fig. 7), with a ciliated epithelial layer, a primitive sacculate gut (*pg*) opening at its anterior end, penetration glands (*sg*) which are usually paired, nerve ganglia (*n*), a pair of excretory tubules (*et*) with flame-cells (*fc*), and a group of germinal cells (*gc*) arising from the inner (usually posterior) wall and coming to lie free in the cavity of the larva. These germ cells are the primordia of the next generation.

The hatched miracidium swims rapidly about in the water by means of its ciliated epithelium. In the event that it comes within the immediate

stimulus, and attempts to penetrate the mollusc. If the larva impinges upon soft tissue, it is able to attach itself and is able to digest its way into the tissues of the mollusc by means of its glandular secretions. This entrance may be through the gills (*Fasciola*) or by way of the head or foot

larvæ of these species are provided with cilia for swimming. ... occurs only in the intestine of the favorable molluscan host after the eggs have been ingested, from whence the free miracidium penetrates into the peri-intestinal lymph spaces of the mollusc.

Once arrived within the tissues of the appropriate mollusc, the miracidium soon reaches a natural lymph channel and may become temporarily

stationed in the head region or may gradually migrate from the oral towards the apical end of the mollusc. Meanwhile it loses its cilia and becomes metamorphosed into a simple sacculate object known as a *sporocyst.* (In some groups, as for example, the family **Echinostomatidæ**, the first generation is a redia.) The sporocyst (Fig. 8) lies bathed in liquid nourishment. It performs all of its metabolic processes by osmosis through its body wall. It has no need, therefore, for the usual organs of digestion, secretion, excretion or stimulation. It is devoted entirely to the

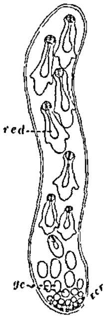


FIG 8

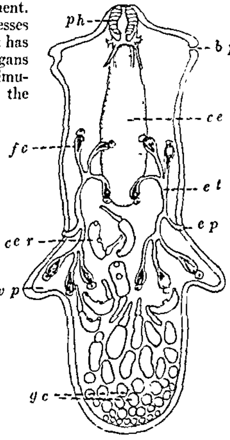


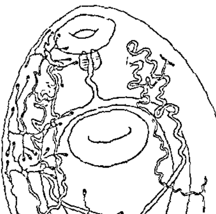
FIG. 9

FIG 8.—First generation digenetic trematode (sporocyst), with second generation (rediæ) developing in the brood cavity; *gc*, germ cells, *red*, redia (Original.)

FIG. 9.—Fully developed second generation of a digenetic trematode (redia), with pharynx (*ph*); rhabdocele gut (*ce*); excretory system, including flame cell (*fc*) excretory tubules (*et*) and excretory pore (*ep*); birth pore (*bp*); evaginate appendages (*evp*), germ cells (*gc*), and developing larvæ (cercariæ, *cer*) of the third generation (Original.)

production and development of its progeny (*gc*). In some species the germ cells which were first observed in the miracidium and have continued to grow as the sporocyst matures, develop into a second generation of sporocysts, more or less like the mother sporocyst. Such is the case with the second intramolluscan generation of the blood flukes. However, in the majority of human trematodes, the second generation becomes modified into a *redia* (Fig. 9), which is provided with a pharynx (*ph*) and an undivided gut (*ce*), as well as a distinct excretory system (*et*), in addition to the posteriorly disposed germinal epithelium (*gc*). Some rediæ also have a birthpore (*bp*) and one or even two pairs of evaginate appendages (*evp*).

While most modern investigators are essentially agreed that the development of digenetic trematodes within the molluscan host is sexual in character, various workers favor different interpretations. The bisexual process described by Woodhead (1931) for gasterostomes possibly represents a primitive condition. Parthenogenesis, as described by Tennent (1904, 1906), may have been a later development. The theory of polyembryony advocated by Brooks (1930) supports the idea of precocious growth of the germ cel[illegible] sitic inse[illegible] argumen[illegible] polyembryony. He states that no ovaries have been acceptably demonstrated in sporocysts or rediæ and that scattered observations on oögenesis have not been confirmed. Of all present-day investigators Stunkard (1936) prefers to regard the phenomenon as an asexual one.



About the time the first generation sporocysts have reached the lymph spaces surrounding the digestive glands of the mollusc, where the maximum amount of nourishment is to be secured, they are gravid with their progeny, which at times number more than a hundred but may be as few as one. The progeny soon rupture the wall of the sporocyst and lie free in the lymph fluid. Here they develop rapidly and their own progeny (those of the third generation) begin to take form. These may be a new generation of rediæ, although in most species of flukes the organisms of the third generation are essentially different from those of the first two generations in that they almost never develop to the adult, egg-laying stage within their molluscan host. Each one is commonly provided with a tail and is known as a *cercaria*, or tailed larva (Fig. 10). The various species of cercariæ also possess various types of secretory

FIG. 10.—Cercaria of *Fasciola*, showing the digestive and excretory systems. The digestive system consists of an anterior oral sucker, within which are found successively an oral cavity, a pharynx, an esophagus and a pair of digestive ceca which end blindly in the subdistal end of the body. The excretory system is composed of a median posterior bladder, with a pore to the outside, a pair of main collecting tubules, each with four secondary tubules, tertiary tubules, and terminal capillaries, each with a flame cell at its inner extremity. (Original.)

glands for use in penetration and encystment, as well as more highly differentiated digestive, excretory and integumentary systems. As few as ten or twelve or as many as several thousand cercariæ may be produced within [illegible] and [illegible] pro- [illegible] od of several months. The cercariæ, when mature, escape from their mother sporocysts or rediæ, either by rupturing the wall or emerging through the birth pore, if the latter be present. By their energetic movements they work their way through the enveloping layers of host tissues and finally lie free in the cavity between the mollusc and its shell. From this region

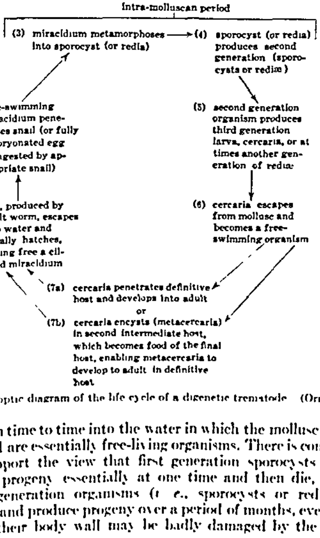


FIG. 11 Synoptic diagram of the life cycle of a digenetic trematode (Original)

they escape from time to time into the water in which the mollusc lives and for a brief period are essentially free-living organisms. There is considerable evidence to support the view that first generation sporocysts typically discharge their progeny essentially at one time and then die, but that many second generation organisms (i. e., sporocysts or rediæ) may continue to live and produce progeny over a period of months, even though in some cases their body wall may be badly damaged by the escaping progeny.

The free-swimming cercaria swims about in the water by means of its tail. In the case of cercariæ with a bifid tail, the caudal organ precedes the body during the act of swimming; in all other cercariæ the body precedes the tail. The cercaria may attach itself by its suckers to the lower side of

the surface film of water or it may sink to rest at the bottom of the water. Sooner or later, usually in twenty-four hours or less, the cercaria must effect measures for active or passive entrance into its definitive host. The blood flukes actively penetrate the tissues of their final host; all other flukes of which the life histories are known enter their final host passively, utilizing a second intermediate host or vegetable tissue or at times even the same molluscan host, in or on which to encyst and await transfer.

Practically all cercariæ are provided with unicellular secretory glands (the so-called cephalic, histolytic, or *penetration glands*) with ducts opening in the vicinity of the oral sucker. These glands secrete a lytic substance which digests host tissue. In the case of the blood flukes this secretion enables the larva to enter its final host; in the case of *Clonorchis*, *Metagonimus* and *Paragonimus*, it enables the cercaria to penetrate into the tissues of a second intermediate host. In many other cases, however, as in *Fasciola* and *Fasciolopsis*, these glands, although present, apparently do not function successfully. The majority of cercariæ are also provided with *cystogenous glands* in the mesenchyma, which are packed with milky granules. After the cercaria has been free-swimming for a longer or shorter time in the *milieu* these granules swell up with water and are secreted as a viscous fluid through minute pores in the integument. Meanwhile the tail is discarded. The cystogenous substance "sets" in the form of an enveloping cyst-membrane around the decaudated larva. The blood flukes lack these cystogenous glands. Encystment of those species which actively penetrate a second intermediate host occurs only after partial penetration of that host has taken place. In other cases it occurs very soon after the cercaria has emerged from its molluscan host. In certain cases, where the molluscan host is the food of the definitive host, the cercaria encysts within the mollusc, and a few cases are known in which the cercaria even encysts within its mother. Thus, these two types of secretory glands (lytic and cystogenous) serve either singly or in coöperation in terminating the free-living existence of the cercaria.

After the cercaria has dropped its tail, and has either penetrated into its definitive host or has become encysted, it ceases to be called a cercaria and becomes the *metacercaria*, which includes the period between the cercaria and the adult. It is also referred to as an *adolescaria*. This stage in the life cycle of the blood flukes covers the period from entrance through the skin of the final host to the maturity of the flukes in the portal blood stream It is both a period of migration and of development. In those species which utilize a second intermediate host there is a passive incubation within this host, followed by a period of migration and development. Those species in which encystment takes place upon plant tissue (*Fasciola*, *Fasciolopsis*, etc.), differ from the latter in that the passive period of encystment is not one of growth for the metacercaria.

Unencysted metacercariæ usually cannot pass through the gastric secretions of vertebrate hosts and live. On the other hand encysted forms are uninjured by their passage through the stomach. On arriving in the medium of the intestinal secretions of the appropriate host, the cyst membrane is digested off or breaks down from the movements of the con-

tained larva, the metacercaria emerges and migrates to the place of its adult residence, where it develops into the adult worm.

The life cycle of the digenetic trematodes is epitomized in the synoptic diagram on page eighty-one (Fig. 11). It is more specifically illustrated for three types of human trematode infections in the following Figs.: *Schistosoma japonicum*, Fig. 16; *Fasciolopsis buski*, Fig. 79; *Clonorchis sinensis*, Fig. 106.

CHAPTER X

THE TREMATODES OR FLUKES. CLASSIFICATION

THE BASIS OF CLASSIFICATION

THE trematode group is a very large one, comprising several thousand species whose relationship to one another is as yet imperfectly understood. For this reason any classification of the group is admittedly unsatisfactory. Much of the difficulty is due to the fact that, in the past, descriptions of all but a few species have been based exclusively on the morphological characteristics of the adult generation, without considering the life cycle of the organism in its entirety. Furthermore, the recognized classification adopted by systematists and commonly found in older text-books is confined to the external features and the reproductive organs, frequently of preserved specimens only. Within recent years an attempt has been made to find other constant structures which might be relied upon to determine the relationships of the various species.

Much has been learned from a study of the life cycle of some of the flukes. For example, although the specific or generic modifications of the reproductive organs of the adult worm cannot be recognized in the sporocyst, redia or in the cercaria, the excretory system, with its tubules, capillaries and flame-cells, has been found to have a relative constancy throughout the entire life cycle. Although it may be more highly elaborated in the adult than in the sporocyst, redia or the cercaria, the fundamental pattern is essentially the same. Cort, Faust, LaRue and other workers have emphasized the importance of this system in determining the relationship of the cercarial, metacercarial and definitive stages of the various species. The excretory system is even now of considerable value in discovering the superfamily and family of many larval forms, although in several of these groups as presently constituted different types of excretory patterns occur,—a situation which forces the phylogenist to assume that convergent evolution has produced phenotypes from a number of originally different groups. Unfortunately the excretory system in most trematodes can be studied satisfactorily only in living material, and then only in species sufficiently transparent to permit the investigator to observe the various parts of the system in a fluke compressed under a microscopic cover-glass. Other structures of an ephemeral nature, such as the penetration glands of the miracidia and cercariæ, are also frequently serviceable in group diagnosis during the larval stages, but these structures are lost during transformation of the cercaria to the adult worm.

While an artificial system of classification has almost nothing to recommend it, a natural system based on fundamental relationships is of the [illegible] particu- [illegible] placed [illegible] infec-tions is sufficient proof of the desire for a dependable system of classifica-

[illegible]

species which are not parasitic in man. Fortunately for the student of medical zoölogy, the majority of the important trematode parasites which infect man have been made the subject of careful investigation, so that their life cycles are for the most part fairly well understood and their relationships to the class of trematodes as a whole fairly well determined.

OUTLINE OF CLASSIFICATION

The classification presented here is an adaptation of the older system, with rearrangements which are necessary because of recent investigations and additions which have to do particularly with the phases in the life cycle other than the adult worm.

The system has been elaborated only in those orders and suborders which contain flukes parasitic in man, but a skeleton outline of the major divisions has been included for purposes of comparison. It must be understood, however, that no attempt has been made to include any of the large number of genera of trematodes which occur exclusively in lower animals and which are not of primary concern to the physician, sanitarian or medical zoölogist.

CLASS TREMATODA RUDOLPHI, 1808

Parasitic organisms; adults covered with a non-ciliated integument; ciliated epithelium usually occurring on larvæ hatched from eggs; suckers almost always present; alimentary canal present except in sporocyst generation of Digenea.

Subclass I. Monogenea Carus, 1863 (nec van Beneden 1858)

[Price (1937) has presented evidence that van Beneden's groups "monogénèses" and "digénèses" were employed as common descriptive terms and not in a taxonomic sense.]

All species ectoparasitic or in excretory bladder or respiratory passages of host; *haptors* (*i. e.*, organs of attachment), consisting of one or more suckers, of which those at the posterior end are powerfully developed; chitinous hooks and anchors almost always present; excretory pores anterior, double; development direct, with relatively simple metamorphosis and with single host. No representatives in man. Example: *Gyrodactylus elegans* v. Nordmann, 1832, on skin and gills of fresh-water fish, *Polystoma integerrimum* (Froehlich, 1791), in amphibians.

Subclass II. Aspidogastrea Faust and Tang, 1936

Parasitic on or in the soft parts of molluscs, or in the intestinal tract of cold-blooded vertebrates. Development probably always direct; larva hatched from eggs having ciliated epithelium (*i. e.*, *Lophotaspis*, with tufts of cilia), or unciliated epithelium (*i. e.*, *Aspidogaster*); adults hermaphroditic, with or without alternation of hosts, oral sucker absent or poorly

developed; ventral sucking organ a powerful adhesive disc, frequently divided into series of sucking cups; intestine a single blind sac. Basic flame-cell pattern of larva: 2[1 + 1 + 1]. All known species belong to a single suborder, *Aspidogastrata* Faust, 1932, which has the characters of the subclass. No human representatives. Example: *Aspidogaster conchicola* v. Baer, 1826, usually found in bivalves (*i. e.*, Lamellibranchia).

Subclass III. Digenea Carus, 1863 (nec van Beneden, 1858)

Almost all speci
or two suckers, of
pores posterior, d
individuals; development complex, with alternation of three or more sexual generations and alternation of hosts. Larva hatched from egg is a ciliated miracidium. All human trematodes belong to this group.

[Stunkard (1946) has brought forth arguments for the suppression of all of the major subdivisions of the digenetic trematodes, including the orders Gasterostomata and Prosostomata, suborders Monostomata ("monostomes are polyphyletic"), Amphistomata ("amphistomes are distomes"), Strigeata and Distomata, as well as the superfamilies within these groups. While there may be cogency in some of Stunkard's thesis, acceptance of his view must be held *sub judice* until cumulative data on the relationships of digenetic trematodes provide an outline of classification which is both phylogenetically accurate and useable.]

ORDER I. GASTEROSTOMATA ODHNER, 1905

Mouth on mid-ventral surface; haptor (*i. e.*, attachment organ) anterior to mouth imperforate; intestine a simple sac; flame-cell pattern of the miracidium: incompletely elucidated, possibly 2[1 + 1]; intramolluscan stages include sporocyst and redia. Cercariae furcocercous, with abbreviated tail trunk and well-developed furcae; in lamellibranch hosts; metacercariae encysted in the nerves, adults present in the intestine of fresh-water or marine fishes. All known species belong to the family **Bucephalidæ** Poche, 1907. No representatives in man. Example: *Bucephalus polymorphus* v. Baer, 1827.

[LaRue (1926) considers that the cercaria of this group shows kinship to the cercarial stage of the Strigeata. (*Vide* infra.)]

ORDER II. PROSOSTOMATA ODHNER, 1905

Mouth at or near anterior tip of body, surrounded by oral sucker. All of the human trematodes belong to this order.

Suborder I. Monostomata Zeder, 1800[1]

Adults hermaphroditic; no ventral sucker present; flame cells of miracidium asymmetrically disposed, with a flame-cell pattern of: 2[1]; com-

[1] Although the suborder STRIGEATA has fundamental characters which justify its recognition as a distinct group, certain "distomes" have apparently been derived from "monostome" ancestors, while other "distomes" are probably phylogenetically related to "amphistomes."

mon in reptiles and birds, and less frequently parasitic in amphibians and mammals. No human representative. Example: *Quinqueserialis quinqueserialis* (Barker and Laughlin, 1911) Harwood, 1939, (in cecum of American muskrat).

Suborder II. Strigeata LaRue, 1926

Adults mostly monecious but some species diecious; anterior haptor or attachment organ almost always present; one or more ventral acetabula usually present; cercarial stage with a bifid tail; flame-cell pattern of the miracidium: 2[1 + 1]; adults parasitic in gut, blood stream or upper respiratory tract of vertebrates.

Superfamily Strigeoidea Railliet, 1919

Adults hermaphroditic; body divided into two parts, the anterior being flattened, incurved, or cup-shaped, bearing the special organs of attachment, the posterior being more or less cylindrical, ovoidal or conical, and containing the major portion of the genitalia (Families Strigeidae and Diplostomatidae), or lacking anterior and posterior differentiation (Family Cyathocotylidae); genital pore posterior; eggs operculate or with polar filament; cercariæ with a true oral sucker and a pharynx; metacercariæ in molluscs, leeches or lower vertebrates, adults in intestine of vertebrates which feed on the second intermediate host.

Type Family STRIGEIDÆ Railliet, 1919

With the characteristics of the superfamily, and with a distinct constriction separating anterior and posterior portions No species reported from man. Example: *Pharyngostomum cordatum* (Diesing, 1850) Ciurea, 1922 (in intestine of cat).

Superfamily Schistosomatoidea Stiles and Hassall, 1926

Adults monecious or diecious, blood inhabiting flukes, without muscular pharynx, with or without anterior and ventral acetabula, eggs non-operculate; cercariæ apharyngeal, with anterior sucker preoral in position, specialized as an organ of penetration, no encysted metacercarial stage, cercariæ on emerging from molluscan host enter definitive host through skin or buccal cavity

Type Family SCHISTOSOMATIDÆ Looss, 1899

Sexes separate, anterior and ventral acetabula present, intestinal ceca reunite posterior to the ovary to form a single stem, parasitic in hepatic portal veins, caval veins and collateral venous circulation of mammals and birds. Human representatives. *Schistosoma hæmatobium* (Bilharz, 1852), *S. bovis* (Sonsino, 1876) (?), *S. japonicum* Katsurada, 1904, *S. mansoni* Sambon, 1907, and potentially probably other species of this and related genera.

Superfamily Clinostomatoidea Dollfus, 1931

Adults hermaphroditic, flattened, apharyngeal, having an excretory system consisting of a primary collecting bladder, tubules and flame-cells and a secondary network of ramified lacunæ; eggs operculate; furcocercous cercariæ developing in rediæ in gastropod host; metacercariæ encysted in fishes or frogs; adults in the mouth, esophagus or respiratory tree of swimming and wading birds and of reptiles.

Type Family CLINOSTOMATIDÆ Lühe, 1901

With the characters of the superfamily. Example: *Clinostomum complanatum* (Rudolphi, 1829) Braun, 1900, from buccal cavity, pharynx and esophagus of herons and gulls, rarely an accidental parasite of the human pharynx.

(Genus Clinostomum Leidy, 1856
genus from κλινω, to incline or bend, and στόμα, mouth)

Clinostomum complanatum (Rud., 1809) Braun, 1901 (syn. *Clinostomum marginatum* (Rud. 1819) Braun, 1899).

Medium-sized fluke with somewhat flattened body, and suckers near one another; oral sucker considerably smaller and bent backwards; pharynx lacking, esophagus short, ceca extending nearly to posterior extremity of body. Genitalia included within posterior half of body. Eggs large, variable in shape but usually ovoidal, with thick shell; miracidium ciliated only at extremities; cercaria furcocercous; molluscan hosts: *Helisoma* spp and possibly other planorbids; second intermediate hosts: various species of fresh-water fishes, definitive hosts: herons, gulls, cormorants, etc., in Europe, North America, Japan, Palestine Incidental infections in man, one from Japan (Yamashita, 1938) and one from Palestine (Witenberg, 1944). Witenberg reported extraction of the worm from the human pharynx following expectoration of blood.

Suborder III. Amphistomata (Rud., 1801) Bojanus, 1817

Adults hermaphroditic, acetabulum highly developed, terminal or subterminal and posterior to the reproductive organs; eggs operculate; flame-cell pattern of the miracidium: *2[1]*; adults with or without a ventral pouch or disk.

Superfamily Paramphistomatoidea Stiles and Goldberger, 1910

Adults with acetabulum caudo-terminal or subterminal; oral sucker and esophagus present; genital pore pre-equatorial; testes one or two, usually preovarial; vitellaria unpaired. Rediæ and adults with a basic flame-cell pattern: 2[1 + 1 + [illegible] the excretory tubules of each o[illegible] ic in the intestinal tract, rarely [illegible] es.

Of the six recognized families of this superfamily, **Paramphistomatidæ** (Fischoeder, 1901) Stiles and Goldberger, 1910; **Gastrodiscidæ** Stiles and Goldberger, 1910; **Opistholebitidæ** Fukui, 1929; **Gyliauchenidæ** Ozaki, 1933; **Cephaloporidæ** Travassos, 1934, and **Microscaphidiidæ** Travassos, 1922, the following two contain human parasites.

Family PARAMPHISTOMATIDÆ (Fischoeder, 1901), Stiles and Goldberger, 1910

Adults without a ventral sucking pouch or disk. Nine or ten recognized subfamilies, of which a human representative is found in the

Subfamily Cladorchinæ Fischœder, 1901.—Body not divided into two parts; oral sucker provided with a pair of retrodorsal diverticula, testes two, deeply cleft. Human representative: *Watsonius watsoni* (Conyngham, 1904) Stiles and Goldberger, 1910.

Family GASTRODISCIDÆ Stiles and Goldberger, 1910

Body of adult usually flattened and divided into a cephalic portion and a caudal portion, the latter in the form of a ventral sucking disk with many large papillæ Human representative: *Gastrodiscoides hominis* (Lewis and McConnell, 1876) Leiper, 1913

Suborder IV. Distomata (Zeder, 1800) Leuckart, 1856

Adults hermaphroditic; oral and ventral suckers present; reproductive organs completely or largely posterior to ventral sucker; flame-cell pattern of the miracidium: 2[1]. The majority of human trematodes belong to this group This suborder contains many thousands of species, which have been more or less satisfactorily placed in family groups

Species of medical importance fall within the following superfamilies

Superfamily Fascioloidea (Stiles and Goldberger, 1910) Faust, 1929

Medium to large flukes, producing large operculate eggs, which are oviposited in the early stages of segmentation. Miracidia developing and hatching in water; with **X**-type pigmented eye-spots; metamorphosing into sporocysts with or without cecum. Typically two or more generations of rediæ. Cercariæ large, robust, active, gymnocephalous, with simple tail, provided with abundant cystogenous material, encysting on vegetation or in fishes, which, when consumed by the definitive host, provide a means of transfer for the metacercariæ and for their subsequent development into mature worms Excretory bladder primitively **Y**-shaped, lateral twigs and capillaries with terminal flame cells derived from an anterior and a posterior branch of the paired secondary collecting tubules, bladder and primary tubules frequently filled with excretory granules Adults in small intestine and biliary passages of mammals

Type Family FASCIOLIDÆ Railliet, 1895

Eggs very large, ellipsoidal, operculate; miracidia bilaterally symmetrical; cercariæ encysting on grass or roots of plants in moist meadows, or in fishes. Adults large, more or less flattened distomes, with elongate excretory bladder reaching nearly to the ovarian plane and with an abundant supply of lateral twigs and capillaries supplying the entire body; with ovary and testes usually lobed or branched; with a short uterus, entirely in front of the ovary. Two of the three recognized subfamilies (**Fasciolinæ** Stiles and Hassall, 1898; **Fasciolopsinæ** Odhner, 1910, and **Campulinæ** Stunkard and Alvey, 1930) contain important human parasites.

Subfamily I. Fasciolinæ Stiles and Hassall, 1898.—Anterior tip of adults distinctly set off from the rest of the body; intestinal ceca profusely branched; sporocyst and redia generations in species of *Lymnæa* and related genera; adults in biliary passages of herbivorous mammals. Human representatives: *Fasciola hepatica* Linn., 1758; *F. gigantica* Cobbold, 1855. A third species, *F. jacksoni* (Cobbold, 1869) lives in the biliary passages of the Indian elephant. Other species, *Fascioloides magna* (Bassi, 1875) Ward, 1917 and *Fasciola ægyptiaca* (Looss, 1896) Sonsino, 1896, occur in the biliary tracts of North American herbivores.

Subfamily II. Fasciolopsinæ Odhner, 1910.—Anterior tip of adults not set off from the rest of the body; intestinal ceca unbranched; sporocyst and redia generations in species of Planorbidæ; adults in intestine of the pig, man, and probably the dog. Human representative: *Fasciolopsis buski* (Lankester, 1857) Odhner, 1902. Other species of this genus which have been described from man are now considered identical with *F. buski.*

Superfamily Echinostomatoidea Faust, 1929

Elongate, moderate-sized flukes, with a well-developed ventral sucker situated only a short distance behind the oral sucker; producing relatively large eggs with small opercular cap, in early stage of development when oviposited. Miracidia with median eye-spot; developing in water; probably metamorphosing directly into first generation rediæ. Cercariæ produced in second generation rediæ; with simple or keeled, unbranched tails; typically with the number and arrangement of collar spines of the adults; encysting in their molluscan intermediate hosts, other invertebrates or vertebrates, or on vegetation, which, when consumed by the definitive host, provide a means of transfer for the metacercariæ and for their development into mature worms. Excretory bladder a pouch-like structure, sometimes coiled back and forth, extending anteriad to the posterior limit of the posterior testis, where it receives the primary collecting tubules, lateral twigs and capillaries with terminal flame-cells derived from secondary and/or tertiary collecting tubules, which are characteristically filled with excretory granules. Fundamental flame-cell pattern of adults: $2[3 + (3)^n]$. Adults in intestinal tract, and less commonly in the bile passages, of vertebrates. The species of this large and inadequately studied group are at present all placed in the family **Echinostomatidæ**.

Type Family ECHINOSTOMATIDÆ Looss, 1902, emend. Poche, 1926.

This has the characteristics of the superfamily. Of the five or more sub-

families which have been created for species of this family the forms parasitic in man are placed in the **Echinostomatinæ**, **Himasthlinæ** and **Echinochasminæ**.

Subfamily Echinostomatinæ Looss, 1899.—Collar united ventrally by a ridge; cirrus sac not reaching posteriad beyond equator of acetabulum. Human representatives: *Echinostoma ilocanum* (Garrison, 1908) Odhner, 1911; *E. malayanum* Leiper, 1911; *E. melis* (Schrank, 1788) Dietz, 1909; *E. revolutum* (Fröhlich, 1802), *E. lindoënse* Sandground and Bonne, 1940, etc.

Subfamily Himasthlinæ Odhner, 1910.—Collar not continuous across venter; collar spines in one row, usually not interrupted on mid-dorsum; cirrus sac long, tubular, reaching far post-acetabular. Human representatives: *Himasthla muehlensi* Vogel, 1933, and *Paryphostomum sufrartyfex* (Lane, 1915) Bhalero, 1931.

Subfamily Echinochasminæ Odhner, 1910.—Collar not continuous across venter; collar spines interrupted on mid-dorsum, cirrus sac small. Human representative: *Echinochasmus perfoliatus* (v. Rátz, 1908) Dietz, 1910.

Superfamily Plagiorchioidea (Dollfus, 1930) emend. McMullen, 1937, emend. nov. (Syn. Dicrocoelioidea Faust, 1929 *Pro Parte*)

Small to moderate-sized flukes, flattened or cylindrical, producing small to medium-sized eggs with rather heavy opercular cap, and fully developed when oviposited. Miracidia metamorphosing in the molluscan host (gastropod or lamellibranch) into sporocysts. Styletted polyadenous cercaria, with slender unbranched tail, lacking eye-spots; produced in second generation sporocysts or rediæ; encysting in arthropod or other intermediate hosts, or possibly remaining unencysted in molluscs or other invertebrate secondary hosts, which, when consumed by the definitive host, provide a means of transfer for the metacercariæ and for their development into mature worms Excretory bladder typically Y-shaped, with relatively long stem; lateral twigs and capillaries with terminal flame cells arising directly from the lateral pair of primary collecting tubules. Fundamental flame-cell pattern of adult worm: $2[(1 + 1 + 1) + (1 + 1 + 1)]$, or $2[(1 + 1) + (1 + 1)]$ This superfamily tentatively includes the following families: **Plagiorchiidæ** Lühe, 1901, emend. Ward, 1917; **Lissorchiidæ** Poche, 1926, **Dicrocoeliidæ** (Looss, 1907) Odhner, 1910; **Macroderoididæ** McMullen, 1937; **Reniferidæ** Baer, 1924, emend. McMullen, 1937, **Haplometridæ** McMullen, 1937; **Lecithodendriidæ** Odhner, 1910, and **Microphallidæ** Viana, 1924. Human representatives have been found only in the **Plagiorchiidæ** and **Dicrocoeliidæ**.

Type Family PLAGIORCHIIDÆ (Lühe, 1901) emend. Ward, 1917

Adults more or less elongated-oval, moderately flattened to rounded organisms, with testes rounded or lobate, side-by-side or one in front of the other and posterior to the ovary Eggs numerous, thin-shelled, operculate, miracidia bilaterally symmetrical, without eye-spots, cercariæ styletted, with simple tail, encysting in arthropods and vertebrates, adults in the intestine, buccal cavity, lungs or oviducts of amphibians, reptiles, birds and

mammals. Excretory bladder Y-formed. Fundamental flame-cell pattern: 2[(3 + 3 + 3) + (3 + 3 + 3)]. Human representatives: *Plagiorchis javensis* Sandground, 1940; *P. philippinensis* Sandground, 1940, and *P. muris* Tanabe, 1922 (experimental infection).

Family DICROCOELIIDÆ (Looss, 1907) Odhner, 1910

Adults leaf-like or more cylindroidal, with testes anterior to the ovary. Eggs relatively small, with thickened shoulder into which the operculum fits; miracidia bilaterally symmetrical, without "eye spot;" cercariæ styletted, with simple, long, lashing tail; cercariæ introduced into the definitive host either along with the molluscan host, or within some second- [illegible] ment; adults [illegible] vertebrates. Excretory bladder Y-shaped, with a long stem. Fundamental flame-cell pattern of adult: 2[(2 + 2 + 2) + (2 + 2 + 2)]. Human representatives: *Dicrocœlium dendriticum* (Rudolphi, 1819), and possibly *Eurytrema pancreaticum* (Janson, 1889).

SUPERFAMILY OPISTHORCHIOIDEA (FAUST, 1929) VOGEL, 1934, emend. nov. (SYN. OPISTHORCHOIDEA FAUST, 1929 *pro parte;* HETEROPHYOIDEA FAUST, 1929 *pro parte*)

Medium- to small-sized flukes, frequently spinose, with poorly developed musculature, with or without "eye-spots" in adult stage. Cirrus pouch lacking; testes behind ovary; seminal receptacle present; metraterm and ejaculatory duct unite to form common genital duct. Eggs small, thick-shelled, operculate. Miracidia fully developed when oviposition occurs but hatch only following ingestion by appropriate mollusc. Cercariae developing in simple rediae without ambulatory appendages; pleurolophocercous or parapleurolophocercous, with "eye-spots," rudimentary acetabula, without stylet but having 2 or 3 rows of short, hook-like spines above the mouth. Excretory bladder typically Y-shaped or with a short stem. Fundamental flame-cell patterns: 2[(1) + (1 + 1 + 1 +1)], *Opisthorchis felineus,* and 2[(1 + 1) + (1 + 1)], *Heterophyes heterophyes.* Cercariae encysting in fishes, adults in intestinal or biliary tract of mammals, birds, reptiles or fishes The described species are classified in the following families: **Opisthorchiidæ** Braun, 1901; **Heterophyidæ** Odhner, 1914; **Acanthostomatidæ** Poche, 1926, and **Cryptogonimidæ** Ciurea, 1933. Human parasites belong to the **Opisthorchiidæ** and **Heterophyidæ.**

Type Family OPISTHORCHIIDÆ Luhe, 1901

Adults usually lanceolate, with weak musculature, transparent or semitransparent, lacking "eye-spots"; with genital atrium immediately preacetabular, lacking a gonotyl. Human [illegible] live in the biliary and pancreatic ducts of vertebrates. [illegible] but human representatives are found or [illegible]

Subfamily I. Opisthorchiinæ Looss, 1899.—Excretory bladder long, triangular, with median anterior blind tubule; uterine coils post-acetabu-

lar, confined between ceca. Human representatives: *Opisthorchis felineus* (Rivolta, 1884) Blanchard, 1895; *O. viverrini* (Poirier, 1886) Stiles and Hassall, 1896; *O. noverca* Braun, 1902, *Clonorchis sinensis* (Cobbold, 1875) Looss, 1907.

Subfamily II. Metorchiinæ Lühe, 1909.—Excretory bladder short; uterine coils partly overlap ceca and extend preacetabulad. Human representative: *Pseudamphistomum truncatum* (Rud., 1819) Lühe, 1909.

Family HETEROPHYIDÆ Odhner, 1914 (Syn. COENOGONIMIDÆ Nicoll, 1907; COTYLOGONIMIDÆ Nicoll, 1907; HAPLORCHIDÆ Travassos and Viana, 1924; STICTODORIDÆ Poche, 1926)

Small to very small flukes, usually ovoidal to pyriform in contour; with ventral sucker typically enclosed in genital sinus containing a muscular cirrus-like sucker (gonotyl); lacking "eye-spots", testes two (or one in a few species). In intestine of higher vertebrates. All known species appear to be facultative parasites of man, but species from the following four subfamilies are the only ones reported in natural infections from the human host.

Subfamily Heterophyinæ Ciurea, 1924.—Acetabulum and gonotyl (genital sucker) of adult on ventral surface, well developed; testes two. Human representatives: *Heterophyes heterophyes* (v. Siebold, 1852) Stiles and Hassall, 1900, *H. katsuradai* Ozaki and Asada, 1925, and *H. brevicaeca* Africa and Garcia, 1935.

Subfamily Metagoniminæ Ciurea, 1924.—Acetabulum well developed, situated in genital sinus, gonotyl (genital sucker) atrophied; testes two. Human representatives: *Metagonimus yokogawai* Katsurada, 1912, *Metagonimus minutus* Katsuta, 1932; *Diorchitrema pseudocirratum* Witenberg, 1929 (syn. *Stellantchasmus falcatus* of Katsuta, 1932), *D. formosanum* (Katsuta, 1932), and *D. amplicaecale* (Katsuta, 1932).

Subfamily Centrocestinæ Looss, 1899.—Acetabulum pre-equatorial, in genital sinus or projecting on ventral surface; gonotyl (genital sucker) in genital sinus, undergoing atrophy, with a fan-like complement of rodlets; testes two. Human representatives: *Centrocestus armatus* (Tanabe, 1922); *C. formosanus* (Nishigori, 1924)

Subfamily Haplorchinæ (Looss, 1899) Poche, 1926.—Adults with anterior portion of body flattened but not dilated, gonotyl (genital sucker) fused in part with the ventral sucker, surrounded by a half-circlet of rodlets; single large testis in place of usual two. Human representatives: *Haplorchis pumilio* (Looss, 1896) (syn. *Monorchotrema taihokui* Nishigori, 1924), *H. taichui* (Nishigori, 1924), *H. microrchia* (Katsuta, 1932), and *H. yokogawai* (Katsuta, 1932)

SUPERFAMILY TROGLOTREMATOIDEA FAUST, 1929, EMEND. 1939

Relatively small to median-sized, fleshy, ovate flukes, having integumentary spines, producing moderately large, broadly ovoidal eggs, with a broad opercular cap and slightly thickened shoulder, in the early stage of development at the time of oviposition. Miracidia without "eye-spots", bilaterally

1929, *S. rodhaini* Brumpt, 1931, *S. margrebowiei* Le Roux, 1933, and *S. intercalatum* Fischer, 1934, as well as *S. incognitum* Chandler, 1926 and *S. faradjei* Walkiers, 1928 (which have been designated as species only on the basis of eggs recovered from fecal dejecta), should, for the present, be regarded *sub judice*.

THE HUMAN BLOOD FLUKES OR SCHISTOSOMES

Family SCHISTOSOMATIDÆ Looss, 1899

General Considerations.—The human blood flukes, like the other members of the family **Schistosomatidæ**, live in the portal and caval venous systems They are usually unisexual individuals of which the male is the larger, more robust, and the female the more slender, more delicate individual. The male is further characterized by having the lateral margins of its body curved ventrad so as to form a long groove or trough, the *gynecophoral canal*, in which the female lies during a considerable part of her life. Occasionally in *Schistosoma mansoni* Vogel (1917) has found female organs, with fully developed oöcytes, but lacking a uterine pore, in male worms. Under normal conditions the worms most commonly reside in the extrahepatic portion of the portal system (Fig. 13) or the caval system, being attached by their suckers to the intima of the veins. Here they feed on the rich blood coming from the intestines; here the females are inseminated by the attending males, and lay their eggs. In the case of *Schistosoma japonicum*, *S. mansoni*, and *S. bovis*, the worms are most usually found in the mesenteric radicles; on the other hand *S. hæmatobium* has a predilection for the vesical, pubic and uterine plexuses, into which the female worm wanders to lay her eggs. In either case the ovipositing female extends the anterior part of her body into the small veins and venules immediately adjacent to the wall of the intestine or of the bladder, so that the eggs are deposited in the smallest venules. Since the transverse diameter of the egg is usually greater than that of the venule into which oviposition takes place, the wall of the vessel is dilated around the egg but between each two eggs it is constricted. Thus, the appearance of a series of these eggs in a venule is that of a number of short sausage links. Sooner or later, in increasing numbers, some of the eggs are carried along with the blood stream into the liver, where they escape from the blood vessel into the tissues of this organ and set up inflammatory processes. Others, particularly those of *S. hæmatobium*, may be carried up the inferior vena cava through the right side of the heart to the lungs, where they are deposited. However, a considerable number, probably a major portion of the eggs, remain in the congested mesenteric or vesical venules, which are blocked by the bodies of the female worms. The majority of these eggs are extruded into the wall of the intestine or bladder. Some remain in the tissues while others are evacuated into the lumen of the organ and pass out with the feces or urine The disease produced by those species whose eggs are evacuated through the tissues of the gut is known as intestinal schistosomiasis; that produced by *S. hæmatobium* is commonly spoken of as urinary or vesical schistosomiasis, or vesical bilharziasis.

Life Cycle of the Human Blood Flukes.—The eggs of the blood fluke are somewhat immature when they are laid by the mother worm. By the time

they have passed through the tissues and are recovered from the feces or urine they are usually mature and at times the vibrating epidermal cilia and two pairs of flame cells of the enclosed miracidia can be observed through the shell wall. On dilution of the feces or urine with water, at a temperature of 25 to 30° C. (77 to 86° F.) the miracidium soon becomes active, its cilia beat rapidly and the larva squirms and churns about until

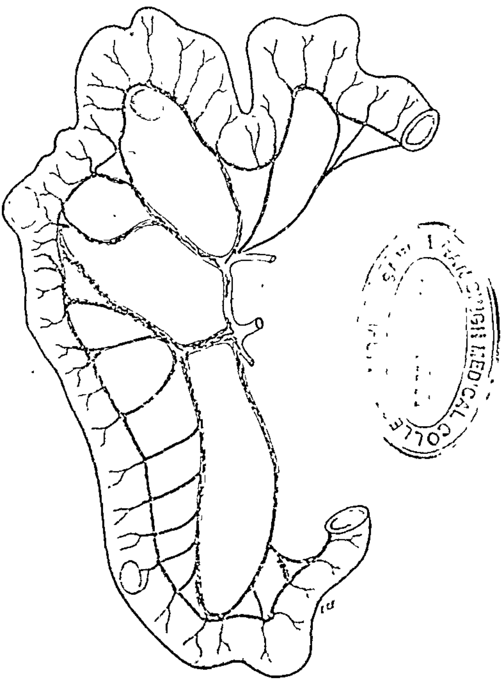


FIG. 13. Loop of small intestine and attached mesentery of dog, showing schistosomes (*Schistosoma japonicum*) in the superior mesenteric venules and veins. (Original.)

the shell splits open at its weakest site, allowing the larva to break through its embryonic envelope and to escape into the water. However, if the excreta remain undiluted for some time, particularly in warm climates, the larva within the shell is killed by the toxic products present or soon developed in the medium. Once the miracidium has been set free in a favorable environment, it is able to swim about as a free-living organism for some hours, utilizing the food-stuffs which it has received from the mother worm. In the event that it finds itself in the immediate vicinity of the molluscan host to which it is physiologically adapted, it attacks and proceeds to penetrate the soft parts of this mollusc. The miracidium possesses no spines or other armature which it can use for this purpose, but the vigorous beating of its cilia once having brought it in contact with a mucus-secreting surface of the appropriate snail, droplets of a viscious lytic ferment which have been elaborated in special glands of the larva are poured out rapidly and soon effect an entrance into the soft tissues of the host. Thus, within a half hour or an hour after the attack has been undertaken, penetration has usually been effected. Schistosome miracidia enter *via* the head, foot, tentacles or the gill filaments of the snail.

The intra-molluscan phase of the life cycle involves the gradual migration of the larva from the oral towards the apical end of the host, at first through artificially produced pathways, later *via* natural lymph sinuses. Meanwhile, within a few hours after effecting penetration through the epithelial covering of the snail and at times possibly not until it has reached a natural lymph space, the larva loses its ciliated epithelium and becomes modified into a simple sacculate sporocyst, which, in turn, produces within its brood cavity a second generation of sporocysts, more elongate than the mother sporocysts. The daughter sporocysts reach the lymph sinuses which bathe the snail's digestive gland, where they are in the midst of a highly nutritious, liquid medium. The second generation sporocysts then produce within their brood cavities a new generation of individuals, which soon become differentiated into fork-tailed larvæ (the cercariæ). They are the larvæ of the third generation. The period required for the intramolluscan phase of the life cycle (*e. g.*, from the entry of the miracidia until the cercariæ are mature) varies under natural conditions from four to seven weeks. Upon becoming mature the cercariæ erupt from the second generation sporocyst, break through the distended tissues of the snail and emerge, tail first, through the opening between the snail and the shell. This occurs only in case the snail is in the water, and in the case of *Schistosoma japonicum* only in bright sunlight.

The cercaria, after issuing forth into the free-living environment, swims about vigorously for some time and then comes to rest at the bottom or attached to the under side of the surface of the water. It is alternately motile and resting for twenty-four to forty-eight hours, after which time it dies unless an opportunity is offered for its transfer to a mammalian host. In heavily endemic areas it is usual to find 1 to 10 per cent or more of the susceptible molluscan hosts infected with the sporocysts and developing cercariæ of the human blood flukes. Once an infection has become established in the snail, cercariæ may be expected to be shed in considerable numbers at regular intervals for a period of several to many weeks.

Entry into the definitive host is an active process for the cercariæ. A susceptible mammal, all or part of whose body comes in contact with "infested water" (*e. g.*, water containing viable cercariæ) is liable to infection (see Figs. 14 and 15). Very few, if any, schistosome cercariæ penetrate the mammalian skin except from contact with a surface film of water. Possibly the largest amount of infection occurs on the extremities of the host, which are alternately immersed and then withdrawn from the water, so that the cercariæ remain in the film of water covering the skin, which soon

FIG. 14.—Common method of acquiring infection with *Schistosoma hæmatobium* and *S. mansoni* in Egypt. (After Faust and Meleney, Am. Jour. of Hygiene.)

FIG. 15.—Common method of acquiring infection with *Schistosoma japonicum* in China. (After Faust and Meleney, Am. Jour. of Hygiene.)

begins to evaporate. This evaporation stimulates the cercariæ to attack and penetrate the skin. It may secure an attachment under exuviae of epidermis or in the depression of a hair follicle. While in the act of entering the skin it maintains contact by means of its suckers. Penetration is effected in a manner similar to that utilized by the miracidium in securing entry into the molluscan host, namely by the discharge of lytic ferments at the head end of the cercaria, which digest away and effect an entrance through the host tissue. This is undoubtedly augmented by the mechanical

erosion produced by the sharp cutting edge of the tips of the penetration-gland ducts, at the sites where digestive ferments are being secreted. Even though the cercaria is armed with abrasive as well as digestive apparatus, its penetration of the skin as deep as the *rete mucosum* requires hours, as compared with the relatively rapid entry of the miracidium into the snail,

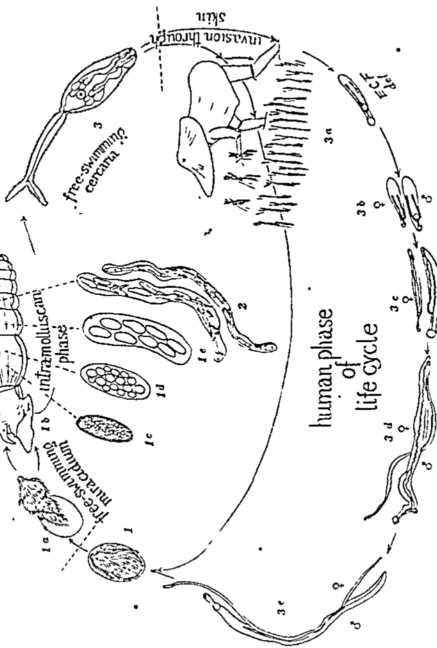


FIG. 18 —*Life cycle of a human blood fluke, Schistosoma japonicum.* *1, 1 a-c*, first generation (*i. e.*, egg→miracidium→sporocyst), *2*, second generation (*i. e.*, sporocyst), *3*; *3 a-e*, third and definitive generation (*i. e.*, cercaria→schistosomulum→adult schistosome) (Original.)

although entry into the epidermis may require less than ten minutes

Shortly before or at the time of initiating the process of penetration the cercaria discards its tail, so that only the body of the cercaria actually enters the mammal. The metacercaria of the mammalian blood fluke is known as a *schistosomulum*. After a period of about sixteen to twenty hours

of active digestion through the skin layers the schistosomulum reaches the peripheral bloodvessels. On entering a venule its active penetration is brought to an end. Thereafter it is carried through the venous circulation to the lungs, where the majority of the migrating worms squeeze their way slowly through the pulmonary capillaries, are carried into the left chambers of the heart, and enter the arterial circulation. Although there is probably no selective migration, the majority of the young worms eventually reach the arteries feeding the abdominal viscera. Of this group apparently only those which enter the mesenteric arteries and pass through to the mesenteric veins are able to develop further. Those reaching the renal and peripheral circulation and probably those in other foci soon die and thus come to assume the rôle of foreign protein emboli at these sites.

The schistosomula first begin to feed after they arrive in the portal vessels, the food consisting of whole blood, although the substance essential for survival and growth appears to be glucose. This is present in relatively high concentration in portal blood. During this active period of growth the young worms live for the most part in the intra-hepatic portion of the vessels, where the males and females soon begin to show recognizable differences, the male becoming broad and stout and the female long and slender. As the [illegible] they migrate out to the mesenteric radicl[illegible] *via* the inferior mesenteric veins, then [illegible]rior hemorrhoidal and pudendal veins into the vesical plexus (*S. hæmatobium*). Shortly after reaching these locations they mate and the females begin to lay eggs. From four to twelve weeks after the cercariæ penetrate the skin, eggs are first recovered from the excreta. The accompanying diagram (Fig. 16) of the life cycle of *Schistosoma japonicum* is typical for the group.

Geographical Distribution of the Human Schistosomes.—Three of the species of human blood flukes, *Schistosoma hæmatobium*, *S. mansoni* and *S. bovis*, appear to have originated in the Nile Valley, from whence they have been dispersed. On the other hand, *Schistosoma japonicum* is confined to the Far East. It is altogether probable that the Yangtze Valley was the original home of this parasite. *Schistosoma hæmatobium*, *S. mansoni* and possibly *S. bovis* have become adapted to related groups of non-operculate gastropods as their intermediate hosts. In South Africa evidence points to the view that the two former species of flukes may utilize the same species of host (*Physopsis*). The species of snails (*Bulinus*, *Physopsis*) in which *S. hæmatobium* develops are relatively common throughout Africa, the adjacent region of Western Asia, and parts of Southern Europe, while the typical molluscan host (*Planorbis*, *sensu lato*) of *S. mansoni* is quite cosmopolitan in its distribution. The species of operculate amphibious snails which *S. japonicum* utilizes for the intra-molluscan phase of its life cycle are common in certain areas of the Far East. Examination of the accompanying map (Fig. 17) shows that schistosomiasis hæmatobia and schistosomiasis japonica are practically coextensive with the distribution of the molluscan hosts utilized by the worms causing these respective infections, while schistosomiasis mansoni has spread only to parts of Africa and the northern part of South Am[illegible] adjacent Caribbean islands

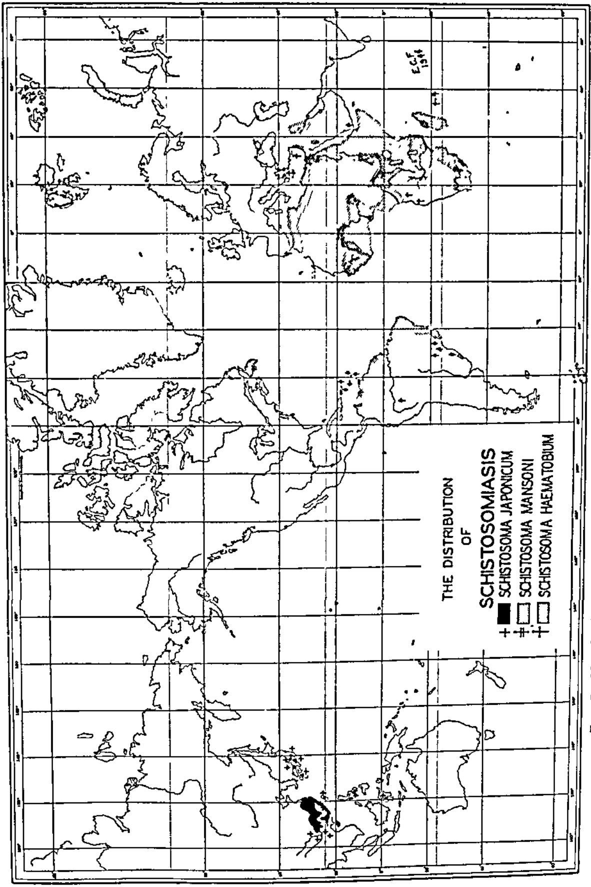


FIG 17 —Map showing the distribution of the human schistosomiases. (Compiled from various sources.)

As more careful taxonomic study is being made of planorbid snails, there is cumulative evidence that only certain closely related tropical species (Ethiopian and Neotropical) are capable of serving as intermediate hosts of *Schistosoma mansoni*. *Schistosoma bovis* has been reported from man only in Natal, South Africa and it is entirely possible that the large terminal-spined eggs recovered from the stool, on which the diagnosis was based, may belong to a variety of *S. hæmatobium*.

CHAPTER XII

THE HUMAN BLOOD FLUKES.

Genus Schistosoma Weinland, 1858
(genus from σχιστός, split, and σῶμα, body)

Schistosoma hæmatobium (Bilharz, 1852) Weinland, 1858.—(The vesical blood fluke, causing vesical schistosomiasis.)

Synonyms.—*Distoma hæmatobia* Bilharz, 1852; *Gynæcophorus hæmatobius* (Bilharz, 1852) Dies., 1858; *Bilharzia hæmatobia* (Bilharz, 1852) Cobbold, 1859; *Bilharzia magna* Cobbold, 1859; *Thecosoma hæmatobium* (Bilharz, 1852) Moq-Tandon, 1860; *Bilharzia capensis* Harley, 1864; *Bilharzia ægyptiaca* Miyagawa, 1924.

Historical Data.—Although there is evidence that vesical schistosomiasis was present in Egypt in ancient times and although the various armies of occupation of this country within modern times, particularly the French in 1799, suffered from the disease, the causative organism, *Schistosoma hæmatobium*, was not discovered until 1851, when Bilharz recovered the worms from the mesenteric veins of a native of Cairo. The first record of the finding was published in 1852. Some time later Bilharz found that this organism was associated in a causal way with hematuria, which was common in the native fellaheen population, and with the presence of eggs in the urine. In 1864 Harley showed that the hematuria of South Africa was due to a blood fluke, which he called *Bilharzia capensis*, to distinguish it from the North African variety, because he found only terminal-spined eggs in the urine of his cases, whereas Bilharz and his colleague Griesinger had figured both terminal- and

(1874–1895), Lortet and Vialleton (1894–1905) and Looss (1894–1914) were all

was incorrect.

As early as 1893 Manson suggested that the vesical and intestinal types of infection were due to two different species. In support of this belief Sambon (1907) proposed a new species name, *Schistosoma mansoni*, for the worm which produced the lateral-spined egg.

The clinical and public health importance of schistosomiasis haematobia in Egypt is indicated by the serious pathological involvement found post-mortem Griesinger (1866) reported this disease in 32 per cent of 363 autopsies, Sonsino ... 500, and Ferguson ... Hospital in Cairo. ... vey of 30,000 indi- ... al basis for a more scientific study of the disease. In 1915 Leiper, who had previously visited Japan and had confirmed the experimental findings of Miyairi, that a mollusc was the intermediate host of *Schistosoma japonicum*, restudied the problem in Egypt and by a series of convincing experimental tests, proved that two types of molluscs were

involved in the Egyptian infection and that those worms which developed in *Bulinus* (*Isidora*), on maturity in mammals, produced terminal-spined eggs, while those which developed in *Planorbis* produced lateral-spined eggs in their definitive host. Leiper also showed that the adult worms of these two types were morphologically different, thus confirming Manson's and Sambon's hypothesis, and demonstrated that those producing terminal-spined eggs (*S. hæmatobium*) were the cause of vesical schistosomiasis while those producing lateral-spined eggs were the cause of intestinal schistosomiasis. Following this McDonagh (1918) first advocated

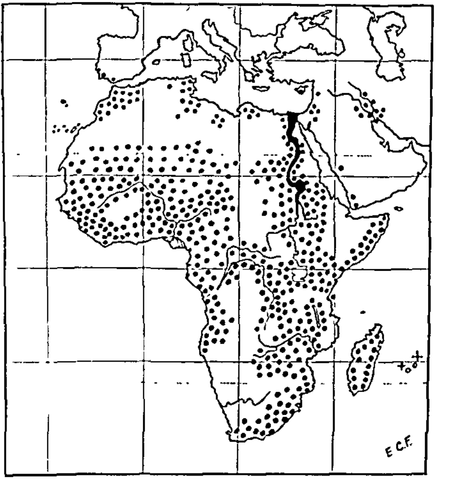


FIG. 18. Map of Africa and environs, showing the endemic foci of infection with *Schistosoma hæmatobium*. The solid area in the Nile Valley indicates extensive hyperendemicity. (Original.)

and Christopherson (1918) introduced on a large scale the use of tartar emetic in the treatment of schistosomiasis. In recent years Khalil and others have combined epidemiological studies with campaigns for prevention and treatment of the infection, while Barlow has devoted many years to epidemiological and preventive work.

Geographical Distribution. Schistosomiasis hæmatobia is extensively distributed throughout Africa (Fig. 18). It is present in a considerable portion of the population of the Nile Valley, where the fellaheen are heavily

infected. In lower Egypt, including the Nile delta, its incidence varies from 11 to 75 per cent. In the Nile valley of Upper Egypt it is found in 4 to 85 per cent of the population of different villages. In the Baharia, Fayoum, Dakhla and Kharga Oases its incidence is 40 to 63 per cent (Barlow and Azim, 1946, 1947). The infection is common in all provinces of the Anglo-Egyptian Sudan, Ethiopia, and along the entire east coast of [illegible] articularly heavy in the [illegible] entral Africa it extends southwards from the Sudan through Uganda (where it is sporadic), Kenya (50 per cent around Lake Victoria), Tanganyika (33 to 94 per cent in [illegible]

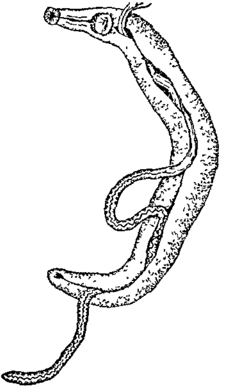


FIG 19 —Male and female specimens of the human blood fluke (*Schistosoma hæmatobium*. × 12 (After Looss.)

the Cameroons. It occurs as a moderately heavy infection in Northern Rhodesia (0 to 60 per cent, *fide* Blackie, 1946), up to 80 per cent in Africans in Southern Rhodesia, and is especially common in populations along the rivers of Natal and Cape Colony. Along the coast of North Africa it extends from Egypt to Morocco. In Africa the monkey, *Cercocebus fuliginosus*, is suspected of being a reservoir host. It is known to be endemic in southern Portugal (three foci on the South Coast) and has been reported from Cyprus (one area only). In Western Asia it occurs in Palestine (Jaffa area), parts of Arabia (Mecca and Yemen), Iraq and Iran (along the Persian Gulf).

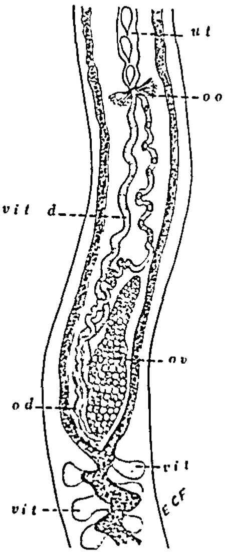
A hyperendemic area of infection has been discovered in northern Syria near the Turkish border (Dr. Alan C. Pipkin, personal communication, 1948).

It is endemic on the islands of Madagascar and Mauritius, but its status on Reunion is *subjudice*. It is also stated to have been diagnosed as an auchthonous infection in India (Punjab Province, by Andreasen and Suri, (1945). Following World War I it became temporarily established in Australia, where two autochthonous cases were discovered, and where snails of the genus *Bulinus*, which are common throughout the settled portions of the continent, may have been the intermediate host. Stoll (1947) has estimated the world incidence of schistosomiasis haematobia at 39.2 million persons, almost exclusively in Africa.

The report of *S. haematobium* infection from Chicago, Illinois, by Sullivan

(1932) and from Seattle, Washington, by Peacock and Voegtlin (1935) were unquestionably due to mistaken diagnosis.

Structure and Life Cycle.—The first careful study of the adult worms and of the miracidium was that of Looss (1896). The worms, which are diecious, live for the most part in the vesical venules and in adjacent plexuses. In ordinary infections the males and females are about equal in numbers. The male is the shorter, stouter individual, while the female is delicate and elongate (Fig. 19). During the greater part of its productive life the female lives in the gynecophoral canal of the male, which is formed by the infolding of the ventral side of the male's body posterior to the ventral sucker. Both sexes possess an anterior (oral) and a ventral (blind) sucker, which are situated close together at the anterior extremity of the worm. In the female these suckers are nearly equal, but in the male the ventral one is considerably larger and more muscular. The integument of the male is covered with minute papillæ, which in the female are confined to the anterior and posterior extremities. In both sexes the esophagus reaches to the anterior margin of the ventral sucker, where it bifurcates to form the ceca. There is no pharyngeal sphincter but the esophagus is surrounded by glands (see Fig. 21). The paired ceca extend to the middle of the body, where they join each other to continue posteriad as a single, zigzag, serpentine trunk which ends blindly near the posterior end of the body. The nervous system is not essentially different from that of other trematodes. The excretory system consists of a small median posterior bladder, with a pair of collecting tubules having equal anterior and posterior tributaries.



Differential Characteristics of Male and Female Worms. The female is a slender worm, measuring about 20 mm. in length by about 0.25 mm in transverse diameter. Her body is grayish or pinkish-creamy in color, while the gut is a distinct reddish-black, like that of a leech, due to inclusion of

FIG. 20. Primary and secondary reproductive organs of female *Schistosoma hæmatobium*. *od*, oviduct, *oo*, oötype surrounded by Mehlis' gland, *ov*, ovary, *ut*, proximal end of uterus; *vit*, vitelline glands; *vit d*, vitelline duct. A seminal receptacle, not shown in the figure, is probably present near the site where the oviduct joins the ovary. (Original.)

hematin and other degradation products of the red blood cells of the host. There is a full complement of female reproductive organs (*Fig. 20*). The *ovary* (*ov*) is an elongate object, narrower anteriorly and broader posteriorly. It is situated in the fork where the two ceca join posteriorly. From its posterior face there originates an *oviduct* (*od*), which immediately bends forwards and after traveling a slightly tortuous course opens into the *oötype* (*oo*). While no seminal receptacle has been described for *S. hæmatobium*, its consistent presence in *S. mansoni* and *S. japonicum* argues in favor of its probable presence in *S. hæmatobium*. From the posterior end of the worm, in alternate positions as far forwards as the posterior end of the ovary, there are *vitellaria* (*vit*) with a single median vitelline duct, which passes under the junction of the ceca and proceeds forwards in a course parallel to the oviduct, finally emptying into the oötype. From the anterior face of the oötype the system is continued as the *uterus* (*ut*), which opens to the exterior through a small genital pore just behind the acetabulum. Naked egg cells from the ovary work their way forwards through the oviduct until they reach the oötype, where they are fertilized, the vitelline cells are added, the shell is secreted and the fully formed egg is pushed forwards into the uterus through a sphincter which regulates the mechanism. The eggs in the uterus nearest the oötype are the least mature, while these nearest the genital pore are the most mature of the uterine eggs. From 20 to 30 of these eggs may be present in the uterus at one time.

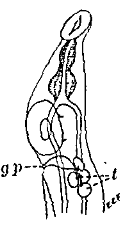


Fig. 21 —Anterior end of male *Schistosoma hæmatobium*, showing reproductive organs *gp*, genital pore; *t*, testes (Original)

The male worm measures from 10 to 15 mm. in length by about 1 mm. in greatest diameter when its sides are in the characteristic incurved position. There are integumentary spines on the suckers and characteristic papillæ over the greater part of the body, particularly on the inner surface of the gynecophoral canal. The reproductive organs (Fig. 21) consist of four to five *testes* (*t*), each with an efferent duct leading into a vas deferens, which enlarges to form a seminal vesicle, before opening to the exterior through the *genital pore* (*gp*), which is situated just behind the ventral sucker. There is no penial organ or other accessory male sexual apparatus.

Adult worms of this species may at times be found in the intrahepatic portion of the portal vessels, in the splenic vein, the pulmonary arterioles, the rectal veins, or rarely even in the cerebral and ophthalmic veins (Faust, 1948). Usually, however, they reside in the tributaries of the inferior mesenteric veins, including the median and inferior hemorrhoidals and particularly the vesical venules and collateral plexuses. Once the worms reach these foci, according to Fairley and Manson-Bahr, "the paired worms travel against the blood stream to the furthermost possible point, where the female leaves her partner, and, being of a smaller diameter, is able by means of her suckers to progress until she stretches the smaller venules to their utmost. The eggs are now depos[illegible]
iorly. The female then withdraws so [illegible]
little in front of the anterior sucker. [illegible]

after the deposition of an egg, the worm retires, the vein contracts to its original dimensions, embracing the egg, and the returning blood drives the spine into the wall of the vein." Thus, by stasis within the smaller vessels, aided by digestive ferments elaborated by the miracidium within the egg, which ooze out through minute pores in the egg shell, the vessels are ruptured and the eggs escape into the tissues. The majority of these finally escape into the lumen of the bladder and are passed in the urine. Occasionally terminal-spined eggs are extruded

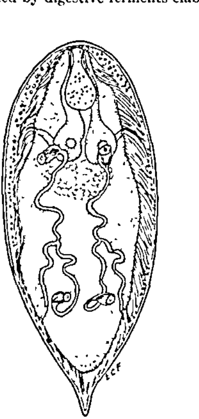


FIG. 22 Mature egg of *Schistosoma hæmatobium* with enclosed miracidium × 640 (Original.)

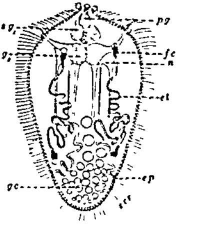


FIG. 23 —Miracidium of *Schistosoma hæmatobium* *ep*, excretory pore, *et* excretory tubule, *fc*, flame cell, *gc*, germ cell, *n* nerve center *pg* primitive gut, *sg₁* anterior penetration gland, *sg₂* posterior penetration gland complex × 400 (Original.)

through the wall of the rectum, particularly during the period when young mature worms are *en route* to the vesical venules

The Egg and the Miracidium. The eggs which are passed in the urine (Fig. 22) usually contain mature, viable miracidia The shells are oval at the anterior end and conical at the aboral end, tapering to a distinct spine. They measure over all from 112 to 170 μ in length and have a transverse diameter of 40 to 70 μ. They are light yellowish-brown in color and fairly transparent. On dilution of the freshly passed urine with 4 parts or more of water the miracidium within soon becomes active, effects a split in the shell, escapes from its enveloping embryonic membrane and emerges as a free-living organism Normal hatching occurs in a non-toxic isotonic medium such as that of the canals, irrigation ditches and ponds in endemic areas Hatching will not occur in undiluted urine If the urine remains undiluted for some hours the larva becomes less and less active and finally dies The emergent miracidium of this species (Fig 23), which averages 150 μ long by 60 μ wide, is typical of the human schistosome group, possessing a ciliated epithelium, two paired groups of penetration glands (sg) one

pair opening at the anterior end and one on the antero-lateral margins, a primitive gut (*pg*), a nerve center (*n*), two pairs of flame cells (*fc*) with tubules (*et*) opening through a single pore (*ep*) on the postero-lateral margins, and germ cells (*gc*) which arise from the germinal epithelium at the posterior end of the larva and are proliferated until they fill the brood cavity. The miracidium of *S. hæmatobium* is distinguishable from that of *S. mansoni* and *S. japonicum* (see Figs. 35 and 46) both morphologically and physiologically. The antero-lateral penetration glands of the larva of *S. hæmatobium* are clearly differentiated into two clusters, while in *S. mansoni* and *S. japonicum* these clusters are fused. The miracidia of *S.*

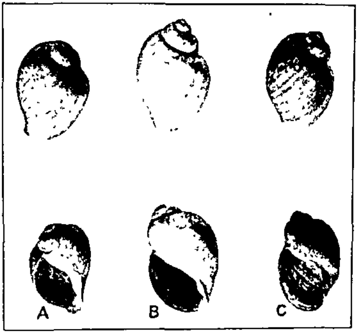


FIG. 24.—Molluscan hosts of *Schistosoma hæmatobium* in Africa. *A*, *Bulinus (Isidora) contortus* from Egypt, *B*, *Physopsis africana* from Natal, *C*, *Physopsis africana globosa* from West Africa Natural size. (Original photographs.)

hæmatobium are equally distributed throughout various levels of the water, while those of *S. mansoni* and *S. japonicum* usually collect in the top 2 or 3 cm. of water These free-living miracidia are able to swim about actively for a period of sixteen to thirty-two hours. During this time they are able to attack and penetrate the appropriate molluscan host. The typical host in the case of [illegible] of the genera *Bulinus (Is*[illegible] e also been incriminated [illegible] appropriate hosts includ[illegible] *B. innesi* (possibly a synonym of *B. dybowskii*), all of which species are referred to by Baylis (1931) as *Bulinus truncatus;* along the north coast of Africa in Cyrenaica and Tunisia, *B. contortus*, *B. brochii* and *B. dybowskii;* on the island of Cyprus, *B. contortus;* in Sierra Leone and other endemic foci on the West African Coast, French Equatorial Africa, Northern Nigeria, Katanga Province of the Belgian Congo, Ruanda Urundi, Tanganyika,

Nyasaland and Rhodesia, as well as in Portuguese E. Africa and South Africa, *Physopsis africana globosa* is actually or presumptively involved; in Northern Nigeria also possibly *Bulinus tchadensis;* in Kenya Colony, *P. nasuta* is suspected; on the island of Mauritius, Portuguese E. Africa, and possibly Kenya Colony, *Bulinus* (*Pyrgophysa*) *forskali;* in Portugal and Morocco, *Planorbis dufourii.* In addition, the infection has been reported from *Bulinus* (*Isidora*) *tropicus* and *Lymnæa natalensis* in South Africa. Furthermore, Dye claims that in Northern Nyasaland *Melania nodocincta* is involved, but this requires confirmation, since melaniid snails are not even distantly related to the typical host species. In Palestine *B. contortus* is known to be involved and in Iraq *B. truncatus* is infected. The molluscan host is not known for the Cameroons, extensive areas of French Equatorial Africa, Italian Somaliland, Ethiopia, Madagascar, Reunion, Arabia and Iran.

There is some evidence suggesting that *S. hæmatobium* has developed specific adaptations to molluscan hosts in different geographical areas. For example, Cowper (1947) reports laboratory-bred *B. truncatus* of Egyptian stock completely refractory to infection with miracidia from a West African strain of the schistosome.

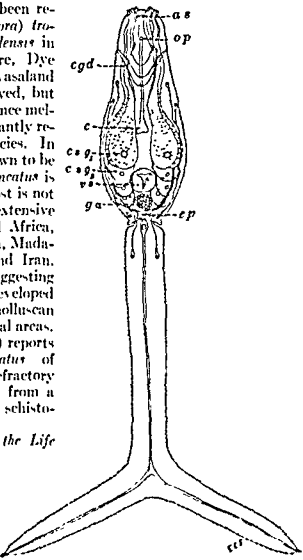


FIG. 25 Cercaria of *Schistosoma hæmatobium*. *as*, orifice of anterior sucker, *c*, cecum, *cgd* penetration gland ducts, csg_1 and csg_2, penetration glands, *ep* excretory pore, *ga* genital fundament, *op* oral pore, *vs*, ventral sucker × 310 (Original.)

Intramolluscan Phase of the Life Cycle Within the mollusc the miracidium is transformed into a smooth-walled sporocyst, which, in turn, produces a brood of daughter sporocysts. Meanwhile the daughter progeny migrate through the lymph spaces of the mollusc and establish themselves in lymph sinuses bathing the digestive gland, where they become greatly elongated and tightly pack the organ According to Leiper (1915) the ends of the second generation sporocysts are solid, but the walls of the tubules are delicate and transparent, so that they invariably rupture when attempts are made to

tease them out of the host tissues. Upon maturity within the daughter sporocyst the bifid cercariæ escape through an opening of the distended integument of their mothers, and are discharged periodically from the mollusc in swarms. According to Archibald and Marshall (1932), cercariæ are discharged from *Bulinus truncatus* over a period of ten to seventy-five days.

The Cercaria.—The cercaria (Fig. 25) of *Schistosoma hæmatobium* consists of an elongated oval body and a tail, which comprises a trunk and two furcæ. When the cercariæ escape naturally from their molluscan host (some six weeks or more after the miracidium first enters the snail) they are always mature. The integument of both body and tail is provided with minute spines. The tail is purely a larval structure, enabling the cercaria to swim about in a jerky, nervous manner during its free existence. On penetration into the definitive host the caudal organ is left behind. Although the cercaria is frequently quiet in an unconfined environment, its measurements are very difficult to determine accurately when under a microscopic cover-glass. Various authors have computed the length and breadth of relaxed specimens as follows: Length of body proper, 140 to 240 μ; of tail trunk, 175 to 250 μ; of furcæ, 60 to 100 μ; breadth of body, 57 to 100 μ; of tail trunk, 35 to 50 μ. The body of the cercaria is provided with an anterior blind sucker (*as*), measuring about 57 to 60 μ in cross-section by 39 to 64 μ in depth. The ventral sucker (*vs*), which is situated in the posterior fourth of the body, is very much smaller. The oral opening is a small pore (*op*) which lies ventral to the anterior sucker. It leads into a capillary tube (the esophagus) which ends in a slightly bilobed pocket (*c*) in the mid-region of the body (the beginning of the furcæ). There is no pharyngeal sphincter. The excretory system is identical with that of the cercariæ of *S. mansoni* and *S. japonicum*. There is a small spherical cluster of genital cells (*ga*) posterior to the ventral sucker. Nerve elements are present posterior to the anterior sucker. The most conspicuous structures in the body of the cercariæ are the penetration glands (csg_1, and csg_2), with their swollen ducts (*cgd*), which open anteriorly through the wall of the anterior sucker. Except for the type and number of these glands and for the somewhat larger size of the cercaria, this stage of *Schistosoma hæmatobium* is not distinguishable from the cercariæ of the other human blood flukes In the case of the cercaria of *S. hæmatobium* (Fig. 25) these organs consist of three pairs of posteriorly situated unicellular glands, with homogenous contents and a basophilic reaction, and two pairs of unicellular glands with granular contents and oxyphilic reaction, situdted just in front of the former. These are in contrast to the four pairs of posteriorly disposed basophilic glands and two pairs of anteriorly disposed oxyphilic glands of *S. mansoni* (Fig. 37) and the five pairs of glands of *S. japonicum* (Fig. 50), see also diagnostic table, p. 164).

Infection of the Definitive Host.—On coming in contact with a mammal, the cercaria penetrates the skin by digesting its way through the layers of tissue, enters the venous circulation either directly or by way of lymph vessels, passes through the lungs to the systemic circulation and, on arrival in the portal system *via* the mesenteric arteries and capillaries, feeds on whole blood, grows, and, after migrating to the vesical venules and col-

lateral plexuses, develops to adulthood. The minimum period of incubation (*i. e.*, that from exposure of the skin to the infective cercaria until the worms are sexually mature in the portal blood), is not less than one month, and is usually ten to twelve weeks, although symptoms of organic disease may not appear until months, possibly two years, later.

Epidemiology.—Infection results from contact with water into which the cercariæ of the blood fluke have escaped from infected snails. In Egypt and other endemic foci practically an entire population may be infected. The distribution of the disease increases as appropriate snails are carried in the waterways into previously uninfected areas, or as human carriers enter uninfected areas where the appropriate snails are found. Farmers, washerwomen and children are all periodically exposed. The religious practices in Mohammedan communities within endemic zones tend to increase both the pollution of the water and exposure to infection. The snails are the more commonly infected because they are sewage-feeders. Their presence and abundance in a particular location is determined by the amount, depth and flow of water, its cyclical increase and decrease, the consistency of the bottom soil and its mineral content, the seasonal succession of aquatic plants and of other fauna, the temperature of the water and the amount of sunlight and shade These combine with the human factors to provide heavy or scanty infection of the snail host, which, in turn, furnishes the "seed" for human infection. In essentially all endemic territory children are more heavily and more frequently infected than are adults. In Northern Rhodesia Blackie (1946) found the percentages of infection to be 45.9 for children and 20.6 for their elders. In Egypt, Scott (1937) found that perennial irrigation from high-level canals is the most important cause of heavy infection.

Pathological and Clinical Aspects of Schistosomiasis Hæmatobia.—Schistosomiasis hæmatobia is commonly referred to in the literature as vesical schistosomiasis, urinary schistosomiasis, bilharziasis, bilharziosis, bilharzia infection, and endemic hematuria. These commonly employed names all refer to the condition produced by the presence of adult *Schistosoma hæmatobium* in the vesical and pelvic plexuses and by the eggs, which are laid by the females and which work their way through the bladder wall and surrounding tissues. As a matter of fact, the first stage of the infection affects entirely other organs and tissues than do the later stages, with characteristic symptoms of toxemia which are similar in all three common types of human schistosomiasis, so that the term schistosomiasis hæmatobia is a more appropriate designation than any of the more commonly accepted names.

The Incubation Period. The first stage of the disease, namely, the *incubation period*, or that of invasion and maturation of the parasite, was studied by Lawton in Australian troops stationed in Egypt in 1916 and by Fairley both in human cases and in experimentally infected monkeys. In addition, there is the case of accidental infection by Cawston, acquired while collecting snails along the banks of infested pools in the vicinity of Durban, Natal More recent information referable to the early period of the disease concerns an American physician, a clinical parasitologist, who during the first week of June, 1944 voluntarily placed 223 cercariæ of *S. hæmatobium* on his skin and nine months later was passing more than 12,000

eggs daily. Eight weeks earlier the eggs were being discharged exclusively in the stools, with subjective and objective evidence between these two dates that the worms were migrating *en masse* to the vesical plexus (Amberson, 1946; Barlow and Meleney, 1949).

. The earliest symptom which has been noted is a tingling sensation of the skin upon coming out of infested water after swimming, or an itching of the skin (Fig. 14) on the part of persons constantly wading in such water. A few hours later small reddish petechiæ may at times be found over areas of skin exposed to the infection for as short a times as fifteen seconds. These minute lesions, which are at the points where cercariæ have penetrated the skin and have reached the peripheral bloodvessels, entirely disappear in the course of a day or two.

No further symptoms occur for a period of three weeks or sometimes as much as twelve weeks, when there is either a gradual or a sudden onset of toxic symptoms, the latter usually being associated with some unusual bodily exertion. These symptoms consists of anorexia, headache, malaise, generalized pains in the back and extremities, and febrile reaction in the late afternoon or evening, frequently accompanied by rigor and sweating. There is commonly an urticarial rash which is most pronounced on the limbs but gradually becomes generalized over the body. Blood examination at this time shows a leukocytosis, with a marked eosinophilia which frequently reaches 50 per cent or more. The abdomen often becomes distended, liver and spleen become enlarged and tender, while sharp pains may be felt in the pericardial region and respiration may become somewhat difficult. There is usually no diarrhea or dysentery in typical uncomplicated cases of schistosomiasis hæmatobia. In areas where natives are constantly subject to reinfection, the uncomplicated symptoms of this period of the disease are difficult to recognize, particularly since urticaria is rarely seen

The lesions produced during the period of migration of *Schistosoma hæmatobium* from the skin to the portal bloodvessels, consisting of hemorrhages in lymph nodes and capillaries and the accumulation of leukocytes around the schistosomula lodged in the subcutaneous tissues, somatic musculature, intestinal wall, kidneys, diaphragm and heart, have not been studied in this infection as intensively as they have in schistosomiasis japonica (Faust and Meleney, 1924) or schistosomiasis mansoni (Koppisch, 1937), but it seems reasonable to believe that they are similar. Nor have the lesions during the stage of maturation of the parasite been studied, except from the indirect evidence of the blood picture and of the generalized toxemia.

The Period of Egg Deposition and Extrusion.—Following the period of invasion and maturation of the parasite is that of *egg deposition and extrusion.* Although the worms are presumably mature and the females are supposedly capable of laying eggs from four to five weeks after exposure to infection, several months may elapse before the bladder becomes involved, and before the characteristic terminal-spined eggs appear in the urine. In Cawston's case eight and a half months intervened between the onset of toxic symptoms and the first appearance of eggs in the urine. During the latter part of this prepatent interval there are usually no special symptoms. The patient may become first aware of the disease by the painless passage

of blood at the end of micturition. This may continue for years without subjective symptoms, during which time eggs are commonly evacuated in the urine. In other cases there are prodromes consisting of headache, backache, lassitude, late afternoon fever and frequent urge to urinate. Such episodes may be of short duration, with symptomless intervals (Ockuly, 1945). Sooner or later, however, a burning sensation is experienced at the time of, and between, the periods of micturition, and the desire to urinate more frequently becomes increasingly felt. In uncomplicated cases dull pains in the loins and suprapubic region, abdominal cramps and sharp colicky pains in the bladder may be experienced. Examination of the inner end of the urethra and the adjacent region of the

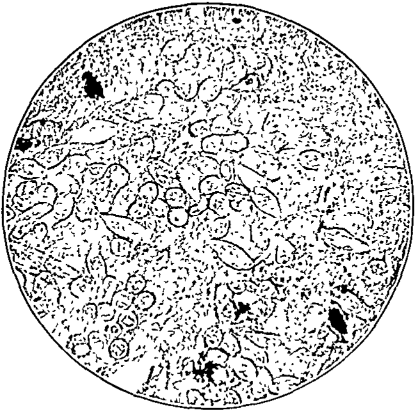


FIG. 26. Photomicrograph of bladder wall infiltrated with eggs of *Schistosoma hæmatobium*. Note large number of viable eggs and a few calcified ones (with black contents). They are trapped in a dense fibrotic matrix in the submucosa. × 100. (Original, Faust, in Craig and Faust's Clinical Parasitology.)

bladder will show involvement of the mucous membranes and frequently the presence of papillomatous folds, which may lead to a misdiagnosis of papillary carcinoma (Miller, 1945). Concretions of uric acid and oxalate crystals are not uncommon in the lumen of the bladder. Meanwhile eggs may have become infiltrated around the prostate or into its tissues, producing induration and causing tenderness of the prostatic region. Even the male generative organs and their tubules may become involved in the general infiltration.

The mechanism for deposition of the eggs of *S. hæmatobium* into the

venules and extrusion into the wall of the bladder and the surrounding tissues has already been described (see pp. 108–109). Fairley has found that as many as twenty eggs may be deposited in a single venule having a diameter much less than that of the eggs, thus giving the "appearance of a string of miniature sausages." The blood current at times drives the terminal spine into the wall of the venule. By means of this weapon, aided by the lytic substances elaborated by the enclosed larva and exuded through the egg shell, a way is made into the perivenous tissues. At first the only changes in the bladder wall are the injection of the small bloodvessels of the mucosa and very minute vesicular or papular elevations of the membrane, which, on microscopic examination, are found to contain eggs, surrounded by giant cells and leukocytes, including large numbers of eosinophils. According to Sorour (1930), the vesical veins may show organized thrombosis with canalization near the worms. When an egg becomes lodged in a venule, it stimulates endothelial proliferation, and subendothelial proliferation when the spine enters the vascular coat. In the muscle coat a typical abscess is formed around the egg. At a somewhat later stage the trigonum vesicæ shows rounded patches of inflammatory thickening, which are superficially granular and full of gritty particles. On section the eggs are found to be abundantly distributed in the muscularis and submucosa and to a lesser extent in the mucosa itself. (See Fig. 26.) Some occlude the bloodvessels. Most of these eggs are viable but some are undergoing calcification. The inflammatory patches on the surface of the bladder may consist of sloughing tissue or phosphatic deposits around eggs, or both.

In addition to the allergic manifestation of urticaria at times experienced by patients during the incubation period of schistosomiasis hæmatobia, this same type of allergy, or bronchial asthma of schistosomal etiology, has been described for the acute stage of the disease (Mainzer, 1938).

The Stage of Tissue Proliferation and Repair.—The third stage is *the stage of tissue proliferation and repair.* It is initiated soon after egg extrusion into the tissues and consists first of all of an increase in the pathological condition of the bladder, including hyperplasia of the wall, so that the symptoms gradually assume the condition of chronic cystitis, aggravated by secondary infection. In the bladder itself phosphatic deposits on the wall become more and more confluent so as to form the typical "sandy patches" The urine changes from acid to alkali in reaction, with an abundance of mucus, pus and blood cells. The calculi in the bladder, which at first consisted of oxalates or uric acid crystals around eggs or a sloughed portion of a papilloma or a blood clot, may now be increased by the depositio [illegible] becomes quite large. Infiltration c [illegible] the mucosa, [illegible] examination very difficult or even impossible.

Meanwhile, the urethra is more and more involved and may become entirely occluded, either from general hyperplasia or nodular swellings or from the attempted passage of purulent débris accumulated within the bladder. Likewise, the lower portion of the ureters may become affected and occasionally involvement may even reach the pelvis of the kidney. Concurrently schistosomiasis of the penis may develop, resulting in indura-

tion of the sheath and an elephantoid appearance of the organ (Figs. 27 and 28) due to obstruction of the scrotal lymphatics. The invasion of pyogenic organisms is not uncommon at this stage, giving rise to perivesical and periurethral abscesses, which break through into the bladder, or produce fistulæ into the rectum, or may involve the entire scrotum and penis in multiple fistulæ. At times pus may ooze out of the scarred and contracted meatus as in gonorrhea. In the female there are similar changes in the vagina. The disease may even involve the uterus.

This stage is accompanied by extreme weakness, emaciation and intense pain in micturition.

The intervals between periods of micturition become shorter and shorter and the amount of urine passed at each period becomes smaller and smaller, finally consisting of little else than pus and blood, which dribble out uncontrolled. With such profound involvement of the entire urinary tract the patient gradually wastes away, or his demise may be hastened by secondary septic involvement.

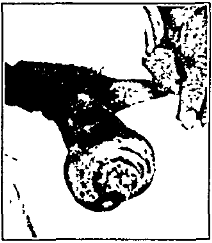


FIG. 27.—Schistosomiasis hæmatobia of the penis, with multiple fistulæ (After Madden, Journal of Tropical Medicine and Hygiene.)

While the primary pathological changes in cases of schistosomiasis hæmatobia involve the genito-urinary system, other organs, particularly the liver, in which eggs have become lodged and are sooner or later extravasated into the tissues, or, at times, even discharged into the biliary tract, partake of the picture of hyperplasia followed by fibrosis and necrotic degeneration. These possibilities must be considered in estimating the damage done in any particular infection. (For the more severe involvement of the liver and spleen in schistosomiasis mansoni and schistosomiasis japonica see pp. 134 and 154, respectively.)

The high coincidence of primary vesical carcinoma and schistosomiasis of the bladder in Lower Egypt has for several decades suggested that the irritation produced by eggs of *S. hæmatobium* infiltrated in the bladder wall may have carcinogenic properties. Ferguson (1913) has shown that in a large number of cases of schistosomiasis hæmatobia in Egypt there are malignancies of the bladder, usually of the posterior wall (Fig. 29), although at times involving the entire organ. Recent studies on this subject have been published by Makar (1941), Scandar (1941), Onsy (1941) and Makar and Fawzy (1947).

In spite of the fact that *Schistosoma hæmatobium* has a special predilection to invade the vesical veins, eggs are occasionally passed from the venules of the inferior mesenteric vessels directly into the wall of the rectum, and are evacuated in the feces, while schistosomal appendicitis, in which partly calcified eggs of *S. hæmatobium* have been found in inflamed foci of the

appendiceal wall, is not uncommon in Egypt (Harris, 1929; Sargent, 1937; Kaufmann, 1937). Less commonly the eggs, or even the adult worms, may be carried to the lungs and the eggs be filtered out in these organs, thus

Fig. 28.—Schistosomiasis hæmatobia of the penis, with elephantoid appearance of the surrounding tissues. (From Byam and Archibald, Practice of Medicine in the Tropics.)

requiring differentiation from pulmonary tuberculosis. Rarely the eggs may reach the brain, spinal cord, conjunctivæ, myocardium or skin and produce symptoms referable to these organs and tissues (Faust, 1948).

ogy.)

Diagnosis.—During the period of invasion and maturation of the parasite no positive diagnosis can be made, although the patient's history and the blood picture may be suggestive of schistosomiasis. Practically all native cases, however, are more advanced when they appear in the clinic. Cystoscopic and digital examination through the rectum will afford considerable assistance, while hematuria is an almost invariable accompaniment of the disease. The finding of *Schistosoma hæmatobium* eggs in the urine following sedimentation or centrifugalization, especially in the last portion voided, is the most definite diagnostic demonstration. At times a biopsied specimen removed from the bladder wall through a cystoscope will provide desirable

confirmatory evidence. It is possible that eggs, recovered from the urine, or even from the feces, and diagnosed as those of *Schistosoma bovis, S. matthei, S. spindale*, etc., may actually have been unusual forms of *S. hæmatobium* eggs. Fairley's complement-fixation reaction (p. 602) is helpful in early cases or in doubtful cases in which eggs cannot be recovered from the urine. Khalil and Hassan (1932) have found an increase in the serum euglobulin in a small percentage of cases, usually those with enlarged spleens. These workers state that the excess of euglobulin is not as pronounced as it is in kala azar, and that it is not related to the severity of the disease nor to the viability of the worms. The disease must be differentiated from renal calculus, from acute nephritis, from benign papillomata and malignant disease of the bladder, hemoglobinuria, oxaluria, and tuberculous lesions of the urinary tract, as well as filarial elephantiasis.

Therapeusis.—*Symptomatic treatment.*—This is not in itself of great benefit, since the long life of the parasite (twenty years or more) makes it likely that continuous extrusion of eggs into the region of the bladder will aggravate rather than simplify the condition.

Antimony tartrates.—Tartar emetic (*i. e.*, potassium antimony tartrate) and sodium antimony tartrate are specific therapeutics and, in cases in which the urinary tract has not been profoundly affected, intravenous injection of these drugs brings about rapid improvement, while a sufficient course of treatment effects a permanent cure. Because of its lower toxicity, sodium antimony tartrate is the drug of choice for intravenous use, and may be given to the majority of cases as out-patients. However, tartar emetic is somewhat cheaper, and is more stable in solution. Khalil and his colleagues in Egypt administer the latter drug in a 6 per cent solution, covering a period of four weeks, as follows:

	Mg of potassium antimony tartrate		
	First visit	Second visit	Third visit
First week	60	90	120
Second week	120	120	120
Third week	120	120	120
Fourth week	120	120	120

Most clinicians prefer to employ a 2 per cent or even a 1 per cent solution of tartar emetic, administering a proportionally greater number of cc's of the drug, in order to reduce irritation of the bronchial epithelium and severe nausea. For a four-week's course of treatment with a 1 per cent solution, administered three times a week, the initial dose is 4 cc., the second is 6 cc., the third is 8 cc., the fourth is 10 cc., the fifth through the fifteenth is 12 cc. each, and the total of 160 cc. contains 1.6 Gm. potassium antimony tartrate (or 0.576 Gm. Sb). If the solution is made up in physiologic salt solution its administration is better tolerated.

Attempts have been made by some workers (Alves and Blair, 1946, with sodium antimony tartrate, Seitz, 1946, with the same drug, and Mills, 1946, with stibophen and anthiomaline) to carry out intensive, rapid treatment. Cawston (1947) states that claims of cure by this procedure "can not bear careful scrutiny, for there is no known way of telling for absolute certainty that all schistosomes have been destroyed once these large blood parasites have gained an entry into the system, except by *post*

mortem evidence." If possible, it is desirable that ambulatory patients remain in a recumbent position for at least one hour after each treatment, to reduce irritation of the lung tissues.

For women and children the dosage is reduced, as it is also when dizziness and vomiting occur.

It must be remembered that tartar emetic is not only a local irritant, but depresses the circulation, respiration, and tonus of the central nervous system. Its use is contraindicated in diseases of the heart, lungs, kidneys, and in advanced hepatic cirrhosis. Experience has shown, however, that death as a result of its administration occurs in only about one-tenth of 1 per cent of treated patients.

For intravenous administration of antimony compounds the usual aseptic precautions must be observed, and great care must be exercised not to allow even a drop of the solution to get outside of the vein, else intense pain, at times followed by sloughing of the surrounding tissues, may result.

Trivalent Antimony Compounds.—For most patients suffering from schistosomiasis hæmatobia the use of the synthetic antimony preparation, neoantimosan (*fuadin, stibophen*) is preferred to that of the previously mentioned antimony compounds. It is claimed to be as efficacious as sodium antimony tartrate, is administered intramuscularly, does not cause irritation and possible tissue necrosis at the site of introduction, and usually produces no nausea, vomiting, coughing, rigors, or detectable damage to the liver. According to Khalil and Betache (1930), a full course of treatment consists in the intramuscular injection of a 6.3 per cent solution as follows: first day, 1.5 cc.; second day, 3.5 cc.; and on eight alternate days, from the third through the seventeenth, 5 cc. (total, 45 cc., containing 0.392 Gm. Sb). More recent evaluation of this preparation indicates that the cure rate with this amount of the drug is relatively low, and that 65 to 100 cc. (containing 0.566 to 0.870 Gm. Sb) must be administered in order to approach the efficiency rating of the antimony tartrates.

Another synthetic trivalent antimonial which has had considerable clinical trial is *anthiomaline* (lithium antimony thiomalate). This is relatively unstable in solution but, like fuadin, has the advantage of intramuscular administration. However, there is no proof that it is superior to fuadin and its cure rate is certainly less than that of the antimony tartrates

Miracil D. This preparation (1-methyl-4-betadiethyl-aminoethylamino-thioxanthone hydrochloride) was developed by Mauss and found by Kikuth and Gonnert to have appreciable therapeutic effect in mice and monkeys experimentally infected with *Schistosoma mansoni.* Hawking and Ross (1948), studying the pharmacology of this drug administered by mouth to human volunteers, found 0.2 Gm. per day to be the maximum tolerated dose. Halawani, Watson, Nor El-Din, Hafez and Dawood (1948) tested its anti-schistosomal effect on 60 Egyptian patients infected with *S. hæmatobium* and *S. mansoni.* Activity was demonstrated only when 10 to 20 mgm. amounts per kilogram of body weight were taken daily for seven to eight days, with a blood level of 300 micrograms per cent. Toxic side-effects included insomnia, headache, giddiness, vertigo, excess sweating, tremors, twitching, abdominal colic, nausea, anorexia, and with larger doses a yellow skin discoloration.

In advanced cases, where the bladder and surrounding tissues have been profoundly affected, specific therapeusis can avail little, and is probably contraindicated. Surgical treatment is indicated in case of bladder calculi, neoplasms and fistulæ, while sulfonamides or other well-known antiseptics may be helpful in clearing up pyogenic infections. In both curable and non-curable cases palliative and tonic treatment is often advisable.

FIG. 30. Schistosomiasis endemic area in Natal, South Africa. *A*, large infected pool at Sydenham; *B*, boys wading in infected pool. (Photographs by Dr. F. G. Cawston.)

Prognosis.—This is usually good in early infections, provided adequate specific treatment is administered in time; fair to poor in chronic infection in which complications have developed.

Control.—All workers agree that infection with *Schistosoma hæmatobium* is acquired through contact with "infected water," and that the infective stage of the organism is the cercaria which has been liberated from the molluscan intermediate host of the fluke. In Egypt, where most consideration has been given to studying the epidemiology of the infection, every province of the country is known to be infected, the incidence of infection (according to a survey quoted by Khalil) varying from 68.4 to 91 per cent. Furthermore, the disease has tended to increase as the irrigation projects from the Nile have been extended into previously arid districts. The distribution of the snails is such as to cause the cercariæ to be present not

ing in the canals and the children bathing in the larger bodies of water, are constantly exposed to the infection, while cercariæ taken into the mouth with raw drinking water constitute an additional hazard.

The vicious cycle is increased the more by the observance of certain religious practices. The Mohammedan religion prescribes that the urethral and anal openings be washed with water after urination or defecation. Male villagers therefore seek the bank of the nearest water course into which they urinate or defecate in order to wash afterwards. Thus a rite, originally intended to foster cleanliness, has been turned into a most dangerous practice. This occurs in spite of Mohammedan condemnation of the pollution of water courses with human excreta, unless the volume of water is large and the flow is considerable, which is not true of most of the irrigation canals.

In South Africa Cawston found that the infested portion of the water courses lies in the pools and along the river banks below the discharge of sewage from towns and cities, ... ıpt to wade about and bathe (Fig. 3 ... Leone where Blacklock studied the p ... were found in pools, below latrines, where the villagers wash and bathe. Thus, the infected areas may be roughly divided into two groups, namely, (1) those in which all of the fresh water is more or less contaminated by infected excreta, and (2) those in which infection is localized in or below community latrines or where sewage enters a water course. All of the data show that the snails involved are sewage-feeders.

With the discovery of tartar emetic as a specific therapeutic, for a period of approximately ten years attempts were made in and around Cairo and Khartoum to decrease the amount of the infection in these areas by *mass therapy*. Thousands of cases were successfully treated, but the constant exposure of individuals to reinfection, and the apparent lack of immunity to subsequent infections on the part of previously infected persons, demonstrated that this procedure was impractical as a single public health measure.

All investigators agree that much good should result from educational propaganda concerning the disposal of excreta. In the Egyptian Sudan it has been recommended that the following measures should be undertaken to prevent the pollution of streams and canals: all waterways near villages

should be fenced; suitable latrines should be provided, and no village should be placed within 300 meters of streams or irrigation projects.

Following the recommendations of Leiper, Khalil claimed that much may be expected in Egypt in concerted attempts to exterminate the snail hosts, utilizing the combined effects of desiccation during the intervals when the canal sluiceways are closed, and treating dry canals with copper sulfate, but Barlow (1935) demonstrated that some of the snails may burrow into the mud and survive attempts at eradication. Moreover, Khalil (1932) has found evidence that *Bulinus* snails reach Egypt from the south, and are carried into small canals and ditches during flood waters. However, the winter closure of irrigation waterways in Egypt does kill many of the snails, even though the majority may survive one hundred and eighty days of drying. Furthermore, the snails which survive several months of desiccation become practically free of blood fluke infection. Thus, the danger from such snails is reduced to a minimum until they, or their progeny, become reinfected from human sources (Barlow, 1935).

Barlow and Abdel Azim (1945, 1946, 1947) emphasize the importance of clearing *Bulinus truncatus* out of small streams by repeated use of hand nets. Areas should first be mapped to determine the presence of the snails, then weeds removed mechanically, after which snails should be scraped off the top layer of ooze with hand nets. Copper sulfate (15 to 50 ppm) should be left to act for three or four days. (Copper carbonate has to be employed in 1,250 ppm for comparable efficiency.)

After more than a quarter century of intensive campaigns in Egypt, beginning with therapeutic prophylaxis, then turning to efforts to kill off the snails by desiccation, sulfation and periodic clearing out of water plants and snails, there are indications that the disease is being brought under control. Another quarter century of continued efforts should result in almost complete eradication of the disease in Egypt.

CHAPTER XIII

THE HUMAN BLOOD FLUKES (CONTINUED).

SCHISTOSOMA MANSONI, S. JAPONICUM, S. BOVIS, S. SPINDALE AND S. INCOGNITUM, THE CAUSATIVE ORGANISMS OF INTESTINAL SCHISTOSOMIASIS. CERCARIA DERMATITIS.

Schistosoma mansoni Sambon, 1907.—(Manson's blood fluke, causing intestinal and hepatic schistosomiasis.)

Synonyms.—*Distoma hæmatobium* Bilharz, 1852, *pro parte*, Bilharz, Looss, *et al*, *Schistosomum americanum* da Silva, 1909.

Historical Data.—In his original researches on human blood flukes in Egypt, Bilharz noted that certain female worms contained lateral-spined eggs Sonsino and Manson both believed such worms to be separate and distinct species from those producing terminal-spined eggs. The observations of Castellani in Uganda (1902) and of Manson (1902), Gonzalez Martinez (1904) and Letulle (1904) in the West Indies served to show a somewhat different geographical distribution of the worms with the two types of eggs.

In 1907 Sambon proposed the species name *mansoni* for the worms producing the lateral-spined eggs, basing his proposal not only on the different size and shape of the eggs from those of the typical *S. hæmatobium*, and the different geographical distribution of the two types, but also on the grounds that the female worms of the two types were different, in that the one only produced lateral-spined eggs, while the other only produced terminal-spined eggs, and, furthermore, on the fact that lateral-spined eggs were only recovered from the feces, while terminal-spined eggs appeared almost exclusively in the urine. Da Silva (1908) first described the greater number of testes in the male *S. mansoni*. The work of Flu (1911) in Surinam and Risquez (1918) in Venezuela served to substantiate Sambon's view and showed that *S. mansoni* lived in the mesenteric veins while *S. hæmatobium* resided for the most part in the vesical and pelvic plexuses. These views were bitterly opposed by Looss, who believed the lateral-spined eggs to be unfertilized varieties of terminal-spined ones However, in 1915 Leiper demonstrated experimentally that the two species were distinct and that the one (*S. mansoni*) was the causative agent of intestinal schistosomiasis, while the other (*S. hæmatobium*) was responsible for vesical schistosomiasis. The data of Chalmers and Pekkola (1917), Lutz (1916–1919) and Iturbe (1917) were all in accord with Leiper's findings.

Geographical Distribution.—Schistosomiasis mansoni (Fig. 31) occurs in the lower Nile delta, where it is particularly common in the male fellaheen population. Girges (1934) reports up to 53 per cent incidence in some
localities. Fro
(0.1 to 0.3 per
widespread in the Upper Sudan, especially in the White Nile Province.
Cicchitto (1938) found a In East Africa it is
found from Eritrea (sca
through Uganda (30 per
17 per cent in the Lake Province area), Nyasaland (20 to 50 per cent), Portuguese E. Africa, Northern Rhodesia (0 to 61 per cent, *fide* Blackie, 1946) and Southern Rhodesia (3 to 16 per cent, widely distributed) and

south to Natal (1.4 per cent). It is frequently recorded from Madagascar (16 to 37 per cent in the south and east). Autochthonous cases are known from the Transvaal. On the West Coast the infection is found in Senegal, the Cameroons, Dahomey, French Guinea and inland to the Lake Chad district (2 to 15 per cent). It is common through the Congo basin, especially in the northeast and lower Congo regions. Preston (1933) reported a focus of infection in Sierra Leone. Cases are recorded for Liberia and

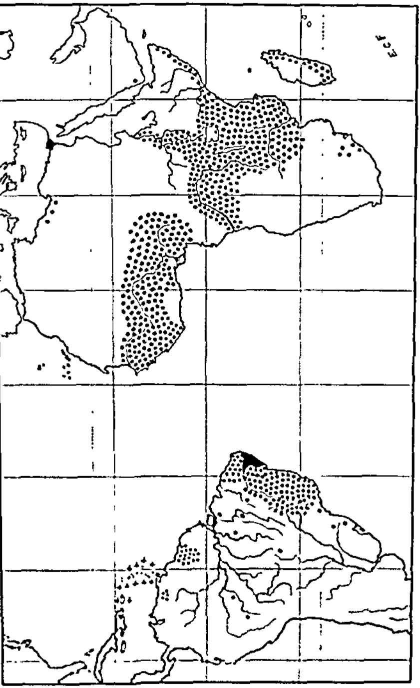


Fig. 31.—Map of Africa, South America and the West Indies, showing endemic foci of infection with *Schistosoma mansoni*. The solid black areas in the delta region of the Nile river and in northeastern Brazil indicate areas of hyperendemicity. The foci in the Lesser Antilles are shown by an +. (Original.)

British Nigeria. Autochthonous cases have been diagnosed in Yemen (Arabia).

In the Americas intestinal schistosomiasis is common in several states of Brazil and Venezuela and occurs in Dutch Guiana. For Brazil Pinto (1945) lists the following states in which the disease is endemic, together with the approximate percentage incidence based on surveys: Pará (3 foci), 0.18–1.9; Piauhy (one focus), 0.5; Ceará (3 foci), 0.22–5.21; Rio Grande do Norte (4 foci), 1.95; Parahyba (11 foci), 2.7–8.0; Pernambuco (65 foci), 3.0–46.0; Alagoas (20 foci), 5.2–52.6; Sergipe (10 foci), 11.8–46.2; Bahia (37 foci, 3.6–33.3; Minas Gerais (33 foci), 7.0–70.0; Espirito Santo (one focus), 3.4; Rio de Janeiro (3 foci), 0.3–1.4; São Paulo (Santos focus), 9.3; Paraná, one focus; Amazonas, one focus; Acre, one focus, and Matto Grosso, one focus. About 2,800,000 persons in the Brazilian foci are infected. (Alves Meira, 1947, states that this estimate is too conservative,

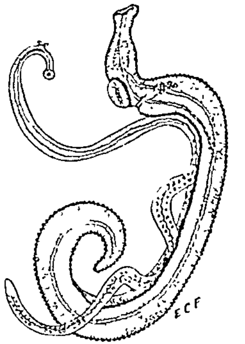


FIG. 32 —Adult male and female *Schistosoma mansoni* in copula × 12 (Original.)

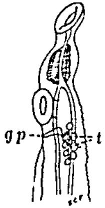


FIG. 33 —Anterior end of male *Schistosoma mansoni*, showing reproductive organs. *gp*, genital pore; *t*, two of the testes (Original.)

since the available data are scanty and in most surveys are based on a single stool specimen per individual or on a single diagnostic technic.) For Venezuela Luttermoser (1945) has confirmed by careful epidemiological surveys the heavy endemicity of the disease in the Valley of Caracas and around Lake Valencia, while there is suspicion that it exists also in Caripe, State of Monagas (Briceño-Iragorry, 1947). Snapper (unpublished report, 1943) found a high incidence of schistosomiasis mansoni in Dutch Guiana (Surinam), especially in rural areas.

It is known to be present in several of the Lesser Antilles, including Guadeloupe, Martinique, St. Lucia, St. Kitts, Nevis, Montserrat, St. Martin, St. Christopher and Vieques. It also occurs as an important infection in several foci in Puerto Rico (approximately 10 per cent of the

island's total population). Its presence in the Dominican Republic (region of Hato Mayor) has been substantiated by Pimental Imbert (1938) and Ponce Pinedo (1942, 1947). No other country in the Americas has been demonstrated to have endemic schistosomiasis. Stoll's estimate of the world incidence of Manson's schistosomiasis is 29.2 million, of which 23 million are allocated to Africa and the remainder to tropical America. Patients with *S. mansoni* eggs in their stools have been reported from North America but no autochthonous case is yet known from this continent.

In Africa schistosomiasis mansoni is frequently coexistent with schistosomiasis hæmatobia, from which it must be differentiated; in the New World it is the only human blood fluke infection.

Structure and Life Cycle.—In general the adult male and female of *Schistosoma mansoni* (Fig. 32) resemble those of *S. hæmatobium*. The female is somewhat smaller than that of *S. hæmatobium*, measuring from 7.2 to 14 mm. in length. The ovary lies in the anterior half of the body just in front of the junction of the intestinal ceca. At the posterior end of the ovary, joining the proximal end of the oviduct, there is a small, retort-shaped seminal receptacle. The vitellaria are more numerous than those in *S. hæmatobium*, occupying the posterior half of the body. On the other hand the uterus is very short and contains one or at most only a very few lateral-spined eggs. The male is also slightly shorter than that of *S. hæmatobium*, having a length of 6.4 to 9.9 mm. The integumentary tuberculations of the male are more prominent than those of *S. hæmatobium* males. The testes number six to nine (Fig. 33) and an equal number of efferent ducts lead into the vas deferens which swells to form the seminal vesicle. The latter organ opens through a non-muscular cirrus tube into the genital pore, which is situated just posterior to the ventral sucker.

Adult worms of this species usually reside in the mesenteric veins. At the time of oviposition the females are characteristically held by the males in the small venules supplying the intestinal wall, where each female deposits an egg, retreats a bit, then lays another egg, and so on, until the venule is distended to the bursting point. The laterally situated spine tends to catch in the intima of the vessel. The obstruction of the vein by male and female worms and the secretion of lytic juices by mature larvae through minute

are soon set free into the intestinal lumen together with a small effluent of blood. As it is recovered from the feces (Fig. 34) the egg is usually fully mature. It is oval at both ends and is provided with a sharp lateral spine. It averages from 114 μ to 175 μ in length by 45 to 68 μ in transverse diameter. The enclosed miracidium (Fig. 35), with an average measurement of about 140 by 66 μ, is somewhat larger than that of *S. hæmatobium* (Fig. 23). The ciliated epithelium and the internal organization are very much like those of the miracidia of *S. hæmatobium* and *S. japonicum*. The most conspicuous difference is the relatively larger size of the anterior pair of penetration glands (*sg*) and of the primitive gut (*pg*), which structures considerably overlap the lateral penetration glands.

When stools containing eggs of *S. mansoni* are diluted with canal or pond

water, hatching occurs rather soon and the miracidia escape through a break in the shell. The free-swimming existence of the miracidium is similar to that of *S. hæmatobium*. On coming in contact with the appropriate molluscan host (Fig. 36), the larva attacks and penetrates the soft tissues of the snail. In Lower Egypt and Eritrea the commonly infected snail is *Planorbis (Biomphalaria) boissyi*. In Upper Egypt and the Anglo-Egyptian Sudan *P. (Biomphalaria) alexandrinus*, *P. (B.) pfeifferi* and *P. (B.) ruppellii* apparently are the most susceptible hosts, although *P. (B.) boissyi* may be occasionally involved. In Nyasaland *P. sudanicus* is reported as the molluscan host. *P. (B.) ruppellii* is also known as an intermediate host in Eritrea and Ethiopia, and the common one in the French Sudan and the Belgian Congo (= *P. adowensis* as reported in the literature for this area). In French Guinea, Sierra Leone, Liberia, Nigeria, Tanganyika, Rhodesia and Natal *P. (B.) pfeifferi* is the common mollusc involved, although *Physopsis africana* and *Bulinus tropicus* are reported as frequently found infected in Portuguese East Africa and the Union of South Africa. In Madagascar the snail incriminated is *P. (B.) pfeifferi* var. *madagascariensis*. The molluscan hosts have not been determined for the Gold Coast ,Dahomey, French Equatorial Africa (including the Lake Chad area), Uganda, Kenya or Zanzibar. The incrimination of *Melanoides tuberculatus* in the Lower Shire District, Nyasaland, requires verification.

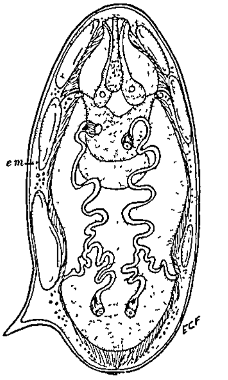


FIG 34.—Mature egg of *Schistosoma mansoni*, with enclosed miracidium viewed from the dorsal aspect, *em*, embryonic membrane × 500 (Original)

In the Western Hemisphere *Australorbis glabratus* is the molluscan host in Puerto Rico, Vieques, the Virgin Islands, Guadeloupe, Venezuela and Dutch Guiana. It is also the sole or predominant host in parts of Brazil, although *Tropicorbis centimetralis* has been found naturally infected in the States of Minas Gerais, Sergipe and elsewhere in the North. *A. antiguensis* is the responsible snail in St. Martin, Montserrat, St. Kitts, Antigua and St. Lucia. Experimentally *Drepanotrema cultratus* in Venezuela and *Tropicorbis "havanensis"* collected in Louisiana have proven susceptible to infection. Cram (1947) suggests that *A. glabratus* is a more recently adapted host than *P. pfeifferi* and that *Tropicorbis* is still more recently becoming an acceptable host.

McQuay (1948) has confirmed the observation of Cram and Files (1946) that *Tropicorbis* sp. from Baton Rouge, La. is experimentally a satisfactory experimental molluscan host, although a closely related species of *Tropicorbis* from Audubon Park, New Orleans appears to be refractory to infec-

tion; while Files and Cram (1948) report that, in addition to the Baton Rouge *Tropicorbis*, *T. havanensis* from Cuba is susceptible to experimental infection.

The development of *S. mansoni* within the mollusc parallels that of *S. hæmatobium*, involving two generations of sporocysts and the eventual formation of cercariæ within the brood cavity of the second generation sporocysts. Lutz (1919), Brumpt (1940) and Maldonado and Acosta-Matienzo (1947) report that the miracidium, entering the snail through the head-foot, tentacles or mantle collar, transforms in two days into a highly convoluted tubule. Beginning on the fourth day numerous daughter sporo- [illegible]

Hoffman (1934) and Gordon, Davey and Peaston (1934) record much slower development of the primary sporocysts and more accelerated growth after the tenth day. The mature cercariæ first emerge from the lymph spaces bathing the digestive gland of the snail about four weeks after exposure to infection (Fig. 37). They are discharged into the surrounding water in the presence of direct sunlight, from about 9 A.M. to 2 P.M., but their emergence is partly inhibited at temperatures of 21 to 23° C., cooler than those prevailing in most endemic areas. They are superficially very much like those of *S. hæmatobium* (Fig. 25). They are somewhat smaller, having body measurements of 185 to 230 μ in length by 75 to 110 μ in breadth; a tail trunk 185 to 300 μ long by 60 to 75 μ in cross-section and furcæ 50 to 75 μ long. The penetration glands of *S. mansoni* consist of two anterior pairs with granular contents and oxyphilic reaction and four posterior pairs with mucoid contents and basophilic reaction. A number of workers have failed to find more than three pairs of glands with mucoid, basophilic contents and believe there are no reliable criteria for the differentiation of the cercariæ of the human schistosomes.

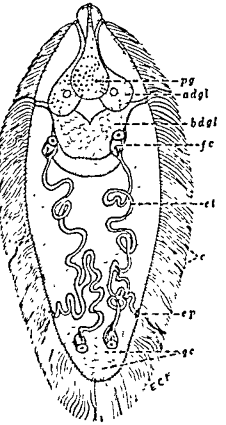


Fig. 35.—Hatched miracidium of *S. mansoni* slightly compressed, dorsal view. *adg*, anterior digestive gland; *c*, cilia; *ep*, excretory pore; *et*, excretory tubule; *fc*, flame cell; *ge*, germ balls; *ldg*, lateral digestive glands; *pg*, primitive gut. × 500. (Original.)

Under optimum conditions the infected snails will continue to discharge cercariæ of *S. mansoni* for many days, even up to two or three months. Faust and Hoffman (1934) have calculated that a single miracidium of this species, which has penetrated into *Australorbis glabratus* and has proceeded

with its normal development without undue injury to the snail, may be responsible for the production of many tens of thousands of viable cercariæ.

The free-living cercaria, following emergence from the snail, alternately swims about vigorously in the water and comes to rest on the underside of the surface films, on objects in the water or at the bottom. It secures no nourishment while in the water, rapidly exhausts its food reserve and must find a mammalian host within thirty hours or die of inanition.

In addition to man susceptible hosts include young dogs, Old and New World monkeys, several species of rodents, especially mice and hamsters, and the armadillo, *Euphractus sexcinctus* (Pinto and de Almeida, 1945).

The method by which cercariæ of this species attack and invade the mammalian host, and migrate through its body to the portal system, does not vary significantly from that of *S. hæmatobium*. According to Pinto and de Almeida (1945) they penetrate at any point on the surface of the skin to which they become attached or enter a hair follicle, lysing cells very rapidly, so that they reach the dermis within fifteen minutes. Once the young worms reach the portal blood and begin to obtain nourishment,

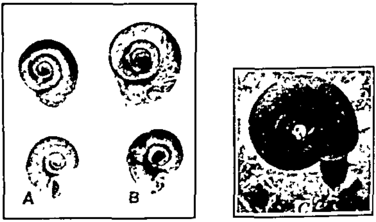


Fig. 36.—Molluscan hosts of *Schistosoma mansoni*. *A*, *Planorbis boissyi* from Egypt, *B*, *Australorbis glabratus* (syn *P guadeloupensis*) from Venezuela, *C*, *A. glabratus*, living snail feeding, from Puerto Rico *A*, *B*, natural size, original photographs; *C*, × 1¼, from Faust and Hoffman, courtesy of Puerto Rico Journal of Public Health and Trop Med.

unlike *S. japonicum*, they do not immediately lodge in the intrahepatic portal vessels, but usually return to the lungs and circulate through the blood stream one to several times before settling down to mature in the portal vessels. The incubation period in the human host is about seven weeks. Previous to the end of this prepatent period the adolescent worms have usually migrated out of the intrahepatic portal vessels, most frequently into ileo-colic and colic branches of the superior mesenteric vein and the colic branch of the inferior mesenteric vein, where they mature, copulate, and the females begin to oviposit.

Occasionally the adult paired worms may travel *via* the accessory portal vessels and be carried to the pulmonary arterioles (Day, 1937, Koppisch, 1937).

Epidemiology.—In endemic zones where the appropriate snails are present in water supplies, promiscuous defecation of infected persons frequently provides the material for infection in the snails. Sewage from towns in

infected foci, emptying into the waterways, adds to the pollution of the water. Since there are no common reservoir hosts, the cycle is characteristically from man to water to snail to water to man. Although urban infection has been demonstrated in Puerto Rico, Venezuela and Brazil, schistosomiasis mansoni is predominantly a rural disease, where human excreta may reach the water near dwellings, in rice fields, irrigation canals in sugar cane plantations or other bodies of water in which the snails abound. In the outskirts of Santos, Brazil infected snails were found in ditches utilized for growing water cress (*Nasturtium officinale*). The disease is contracted by contact with water containing the free cercariæ of this blood fluke. This may occur while wading, swimming or washing clothes in infested water. Usually children and adult males are more commonly infected but in Northern Rhodesia there are more infected females. City water supplies in endemic areas are not necessarily protected by sand filtration or aluminum sulfate clarification, although Witenberg and Yofe (1938) state that the cercariæ of human blood flukes are killed by chloramine, sodium hypochlorite or gaseous chlorine treatment of water. Residual chlorine of one or more parts per million provides a safety guarantee for drinking or bathing water.

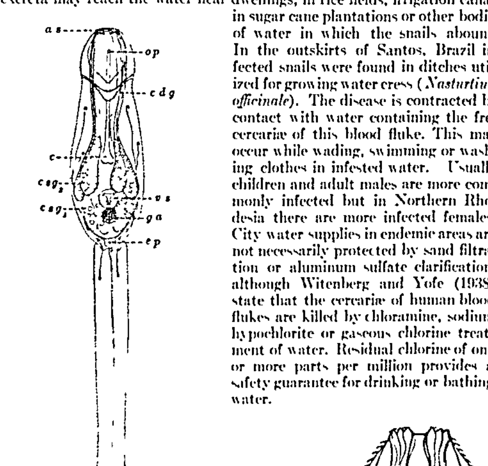


Fig. 57. Cercaria of *Schistosoma mansoni*. × 300. A, anterior end of cercaria, enlarged, to show openings of penetration gland ducts. Lettering as in Fig. 25. (Original.)

Pathological and Clinical Aspects of Schistosomiasis Mansoni. The disease produced by the presence of *Schistosoma mansoni* in the portal vessels is commonly referred to as intestinal schistosomiasis. The clinical picture and the pathological anatomy are in most respects comparable to those of schistosomiasis japonica and are usually distinct from those of schistosomiasis hæmatobia except during the *incubation period*, when the symp-

toms of toxemia appear which are common to all three infections, consisting of remittent late-afternoon fever, cough at night which is frequently non-productive, facial edema, urticaria, abdominal pain, anorexia, rigors and labored breathing. Repeated exposure to infection appears to lessen the allergic reactions. The blood picture at first shows a leukocytosis and frequently a profound eosinophilia (40 per cent or more). At the end of this period of incubation a toxic diarrhea is a characteristic prodromal symptom, followed by dysentery shortly after the extrusion of eggs from the intestinal wall. The eggs are relatively few and are not equally distributed throughout the fecal mass, but are most commonly found in the flecks of bloody mucus which are voided after the fecal matter is passed.

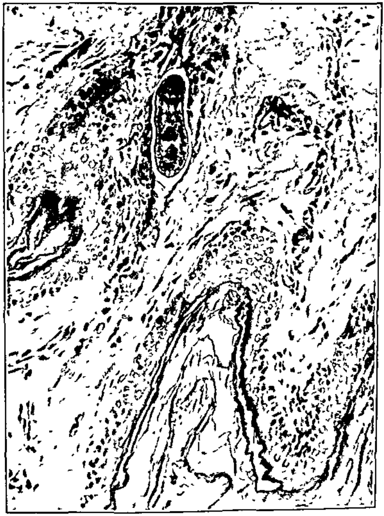


FIG. 38.—Photomicrograph showing metacercaria of *S. mansoni* (*i. e.*, decaudated cercaria) digesting its way into the deeper layers of the skin of an experimental dog. × ca 500. (Courtesy Doctor Cesar Pinto, Instituto Oswaldo Cruz, Rio de Janeiro, Brazil.)

The *second period,* which begins with the *deposition and extrusion of eggs* into the intestinal lumen (according to Pons, 1937, about thirty-seven to forty-four days after initial exposure to infection), is accompanied by irregular dysentery, the so-called *schistosomiasis dysentery,* and a gradual involvement of the liver and spleen. The dysenteric symptoms consist of

abdominal pains and the frequent passage of stools composed of a small amount of fecal matter and considerable blood-stained mucus, the latter usually containing the lateral-spined eggs. This picture is later frequently complicated by a prolapse of the rectum. The liver is enlarged and tender and the spleen becomes passively engorged. In uncomplicated cases the urine is negative for albumen and sugar, and only occasionally contains the lateral-spined eggs. (In 4799 cases of schistosomiasis in Cairo in 1923, in which eggs were detected in the urine, three cases with *Schistosoma mansoni* eggs were found.)

FIG. 39.

FIG. 40.

FIG. 39.—Colon in case of advanced schistosomiasis mansoni with papillomata at left, healthy tissue at right. (After Richards, Journal of Tropical Medicine and Hygiene.)

FIG. 40.—Schistomiasis mansoni lesions of anus and surrounding tissues. (After Madden, Journal of Tropical Medicine and Hygiene.)

The condition which has just been described is caused by the escape of eggs from the mesenteric-portal vessels, including both the mesenteric vein and the intrahepatic portion of the portal system. The presence of these eggs in the tissues of the gut is responsible for rapid development of a pseudo-abscess by infiltration around each egg of eosinophils, macrophages, frequently epithelioid and giant cells, and then fibrocytes. Miliary lesions of this type lead to a thickening of the bowel wall and an excess of mucus production. At first these pseudo-abscesses break through the mucosa to the surface, causing minute hemorrhages with the discharge of bloody mucus, cellular detritus and eggs. The minute ulcers frequently become quite extensive, particularly if secondary infection develops. On the serosal surface the inflammatory process may extend to the peritoneum, resulting in hyperemia of the layer and at times in hemorrhages, with fibrous adhesions. The mesenteric lymph glands are also frequently infiltrated

with eggs, and become hyperplastic. In early cases the posterior ileum, as well as the cecum, colon and rectum, are commonly involved, but later the large bowel bears the brunt of the infection. The eggs which are carried to the liver and escape perivascularly into the tissues produce minute localized lesions, consisting microscopically of pseudo-abscesses and pseudotubercles around the eggs. Hematin pigment has also been found by Fairley and by the present author in various phagocytic cells. The eggs may escape into the lungs, stomach, pancreas, spleen, kidneys, lymph glands, suprarenals and myocardium, where they set up similar reactions, while in one case Müller and Stender (1930) have reported numerous pseudotubercles in the spinal cord, centered around eggs of this species.

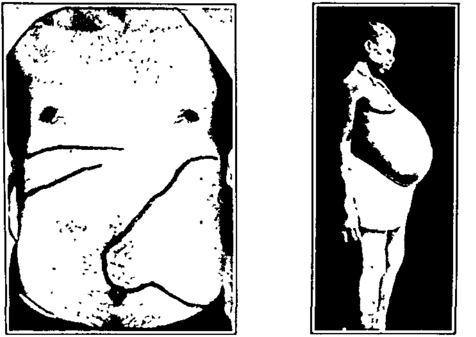
The third period of the infection, that of *tissue proliferation and repair*, is marked by the production of papillomata of various sizes and shapes along the entire intestinal tract (Fig. 39) from the ileum to the anus, thickly distributed or sparsely scattered. The dysentery usually subsides somewhat, but at times there are frequent fecal evacuations accompanied by tenesmus. The pathological picture of the intestine during this period is that of irregular thickening, with massive increase in fibrous tissue. Cicatrices may appear along the length of the intestine, particularly in regions where the wall has become thickened and packed by the schistosomiasis abscesses. In late cases the sphincter ani becomes patulous, allowing masses of pedunculated tissue to protrude (Fig. 40). Fistulous tracts may extend into the ischio-rectal fossa, the perineum, the buttocks or even into the bladder area. Ulceration and epitheliomatous growths in this region are dangerous complications. Splenomegaly and hepatic cirrhosis, with or without ascites (Fig. 41), is a concomitant symptom in a certain percentage of cases and is by no means uncommon in children. In case compensatory dilatation of the collateral circulation occurs, ascites may not develop (Pons, 1937). The most serious development is hepatic cirrhosis, which Symmers has referred to as a "clay pipe-stem cirrhosis," on account of the thickening of the larger veins of the liver, due to toxic secretions of the worms and eggs and to passive congestion. With this is associated the production of scar-tissue in all inflammatory foci. Rarely the gall bladder may become involved, with pseudo-abscesses developing around infiltrated eggs (Haskin, 1934).

Myocarditis resulting from the infiltration of *S. mansoni* eggs into the myocardium may complicate the clinical picture.

The studies of Hernández Morales (1945) indicate that the intestinal lesions of schistosomiasis mansoni in Puerto Rico are usually much less severe than in Egypt or other hyperendemic foci in Africa, where polyposes and papillomata are commonly encountered. Only 5 of 255 patients studied exhibited papillomata of the rectum at proctoscopy, while 50 per cent presented small petechial hemorrhages on the mucosal surface. These observations are in accord with those of Valencia Parpacén and Jaffé in Venezuela.

Koppisch (1943) has provided a clear picture of the sequence of events in the development of the schistosomal pseudotubercle. The egg laid in the lumen of a small blood vessel is surrounded by endothelial lining cells. Rather than remaining occluded, the course of the vessel is temporarily

modified around the obstruction and new anastomoses develop. By inflammatory reaction, lysis from secretions of the mature miracidium within the egg shell and by necrosis, the egg escapes through the wall of the vessel into perivascular tissues. If the egg is in or near the intestinal mucosa, the same factors supplemented by intestinal peristalsis allow the egg to escape into the lumen of the intestine. If the egg becomes impacted in tissues, pseudotubercle formation usually occurs. This may be initiated by neutrophilic infiltration, but is characteristically a process of eosinophilic, monocytic, lymphocytic, epithelioid and frequently giant cell envelopment, with eventual fibrosis and calcification of the egg.



A B

FIG. 41. Schistosomiasis mansoni. A, Early third (chronic) stage. The liver has become somewhat cirrhosed, while the spleen is notably enlarged. Most of the pathology is located in the large bowel. This milder type of intestinal schistosomiasis is more frequent in schistosomiasis mansoni than in *S. japonica*. (Photograph by courtesy of Dr. Juan A. Pons, San Juan, P. R.) B, Advanced chronic stage with marked ascites from the Belgian Congo. (Photograph by courtesy of Dr. Howard A. Bosler.)

Alves Meira (1942) has described the following types of pulmonary complications in schistosomiasis mansoni: (1) Acute toxic type, following the migration of metacercariae through the lungs; (2) bronchopulmonary type simulating late tuberculosis; (3) with endarteritis of the pulmonary arterioles, and (4) cardio-pulmonary form, terminating in congestive heart failure. The more chronic manifestations, resulting from egg deposition in the peri-arteriolar tissues of the lungs, is probably a much more common complication of this disease than is realized. For comparison, Shaw and Ghareeb reported pulmonary lesions in 33 per cent of their cases of schistosomiasis hematobia in Egypt, Koppisch in 10.8 per cent of Manson's infection in Puerto Rico and Jaffé in 24 per cent of the same disease in Venezuela (Jaffé, 1944).

Ectopic lesions, resulting from the deposition of eggs in venules and their escape into peri-venous tissues outside the abdominal viscera and lungs, have been reported clinically and on biopsy or post-mortem examination from the brain, spinal cord and skin (Faust, 1948).

In Egypt, Girges (1934) has stressed the importance of the clinical syndrome produced by male worms unaccompanied by females. Here the damage is purely toxic in nature, due to the secretions and excretions of the worms, and is uncomplicated by [illegible] tissues. In Puerto Rico, Pons [illegible] variety, without essential involvement of the liver and spleen, but he has failed to find an exclusively hepato-splenic type.

It must be borne in mind, as Pons (1937) has emphasized, that the economic and physical condition of the patient contributes in no small measure to the clinical picture of this disease. Malnutrition or overindulgence in food or alcohol reduce his resistance to this, or to intercurrent infections.

Diagnosis.—During the period of invasion and maturation, diagnosis is the same as that for schistosomiasis hæmatobia; during the period of dysentery, specific diagnosis is based on the finding of lateral-spined eggs in the stool.

During the incubation period the symptoms may suggest a highly intoxicative process, with flushed, edematous face, late-afternoon fever, [illegible] -domi- [illegible] eriod [illegible]. In other cases there may be no significant findings. As the acute stage develops there is increased intestinal discomfort, frequently blood in the stool, continuing enlargement of an excruciatingly tender liver and splenomegaly. The clinical picture of the late stage differs from atrophic hepatic cirrhosis of Lænnec in that the spleen in Manson's schistosomiasis is tremendously enlarged, much more so than can be accounted for by engorgement d [illegible] area provides [illegible]

Laboratory [illegible] firmation of presumptive clinical diagnosis of Manson's schistosomiasis. These are: (1) stool examination, including direct films of feces, blood and mucus, concentration and hatching technics; (2) examination of rectal scrapings, aspirates and biopsied specimens, and (3) immunological and serological tests. Each of these will be considered briefly and reference made to more detailed information included in Section VII.

Stool examination involves not only the feces but also flecks of blood and mucus frequently wrapped around formed feces or present in unformed specimens. Because the number of eggs laid by each female *S. mansoni* per day is small, at least 10 Gm. and preferably a larger sample should be available. Special attention should be directed to the examination of flecks of mucus and cellular detritus which are more likely to contain nests of eggs. In addition, there should be routine examination of three to five fecal films, but negative findings on unconcentrated preparations should by no means be regarded as final. Ten to twenty-five Gm. specimens of the stool should be thoroughly comminuted in nine-fold as much water contain-

ing 0.5 per cent glycerine, allowed to sediment, decanted and re-sedimented two or three times, and then a small amount of sediment withdrawn in a pipette and carefully examined. A very useful substitute is the HCl-Na_2SO_4-Triton-ether concentration technic, which fails only if the small sample of feces utilized contains no eggs. $ZnSO_4$ centrifugal flotation is not satisfactory for *Schistosoma* eggs. Some workers prefer the hatching technic originally described by Faust and Meleney (1924).

Rectal scrapings, aspirates or biopsy, first demonstrated by Ottolina and Atencio (1943) and later improved by Hernández-Morales and Maldonado (1946), at times provide positive diagnosis when the feces are repeatedly negative.

Immunological and serological tests, including intradermal reaction, precipitin test, complement fixation and the aldehyde test for excess englobulin, as well as pronounced eosinophilia, are valuable adjuvants but are not helpful until the infection has become well established.

Therapeusis.—Tartar emetic and fuadin are comparably effective in cases of *Schistosoma mansoni* as they are in *S. hæmatobium* infection. The dosage and method of administration are essentially the same (see p. 119), but greater care should be exercised as regards the reaction of the patient to the drug, because of the greater damage to the liver caused by the disease. Pentavalent antimonials, as urea stibamine (Hernández-Morales, Oliver-Gonzalez and Pratt, 1946), have proven too toxic for average tolerance. In the light of present knowledge it seems advisable to recommend the administration of potassium or sodium antimony tartrate, in concentrations not in excess of one per cent, three times weekly until approximately 0.5 Gm. Sb has been given. Magalhaes and Dias (1944) have called attention to the fact that antimony causes extreme dilatation of the walls of the cardiac vessels, with decrease in volume of blood to the coronary arteries. Papillomata of the rectum frequently require surgical treatment. Cases with advanced hepatic cirrhosis are usually not benefited by administration of antimony. Splenectomy should not be undertaken unless there is evidence that the enlarged spleen is definitely embarrassing hematopoiesis. Ascites may require diuretics and paracentesis.

Prognosis.—Fair to good in early or light infections in which the liver and intestinal wall are not seriously involved, provided specific therapy is undertaken in time and is continued until the infection has been eradicated, poor when extensive fibrosis of the liver and bowel wall have already occurred. *S. mansoni* may persist for a period at least up to twenty years (Di Giacomo and Mayer, 1944), producing increased tissue repair by fibrotic replacement.

Control.—Serious study of the public health aspects of *Schistosoma mansoni* infection has been made in Egypt concurrently with *S. hæmatobium* infection, and in Puerto Rico, Venezuela and Brazil, where only the one species of human blood fluke occurs. The molluscan host commonly lives in quiet channels or irrigation ditches and for this reason the field laborers are the class most usually affected. At times, however, where the village water supply becomes involved, or village children wade in infested water, epidemics may break out. The same measures which apply to the prevention of *S. hæmatobium* infection are applicable to schistosomiasis mansoni

Jansen (1946, 1947), in Pernambuco, Brazil, a highly endemic area, has obtained moderate control by instituting the following measures: (1) Destruction of snails with calcium hydroxide, 4 to 5 parts per 1,000; (2) reduction in dissemination of *S. mansoni* eggs by treatment of patients with tartar emetic (one per cent sol.), and (3) construction of public baths and laundry tanks, as well as sanitary drainage canals. The fact that the West African green monkey (*Cercopithecus sabæus*) is a reservoir of this infection in Africa and in the Lesser Antilles (St. Kitts and Nevis) makes the problem of eradicating this organism a more difficult task in these countries

Schistosoma japonicum Katsurada, 1904.—(The Oriental blood fluke, causing intestinal and hepatic schistosomiasis of the Orient.)

Synonym.—*Schistosoma cattoi* R. Blanchard, 1905.

Historical Data.—The earliest record of the disease produced by *Schistosoma japonicum* was that of Fujii in Japan, in 1847. Baelz (1883) made an epidemiological survey of the schistosomiasis endemic area near Okayama, Japan and described the symptoms of the disease, but attributed them to *Clonorchis* infection Yamagiwa (1890), Kurimoto (1893) and Fujinami (1904) all found the eggs of the then undescribed parasite in various organs of individuals who had died of the disease and recognized their etiological rôle in the disease. Kasai (1903) first found the eggs in the feces. Fujinami (May, 1904) obtained a single female worm in the portal vein of a man, which was probably the first adult specimen found Katsurada (April, 1904) investigated the infection in the Yamanashi endemic area and from a study of the symptoms in 5 patients, from whom he had obtained the eggs, suggested "that the disease was caused by these eggs and the mother worms, and that

japonicum

parent worm

One montl

vessels of a Chinese who had died in Singapore. Blanchard christened this

S. cattoi, but it was soon found to be identical with *S. japonicum*. The same year Logan found the eggs of this fluke in Chinese patients in Hunan Province, China

Following these pioneer investigations m ... studied the infection, investigating the morphology of the distribution of the disease in Japan. I

cattle and horses were natural hosts, as well as man, dogs and cats, and by critical experiments proved conclusively that the skin was the usual portal of entry of the infective stage for man. Miyagawa (1912–1913) studied the route of migration through the body, finding that the organism utilized the venous circulation *en route* to the lungs, thence *via* the systemic vessels to the mesenteric system, and finally through the mesenteric capillaries into the portal blood. Meanwhile Miyairi and Suzuki (1913–1914), working in the Kyushu endemic area of Japan, first showed that the fork-tailed cercariæ, which had developed in small amphibious snails (*Katayama nosophora*), were the infective stage for mammals and further observed the hatching and penetratic

of snail, and the developme

stage within this mollusc

verified the obligatory rôle

1915 Leiper and Atkinson confirmed this work.

Various physicians in China, including Logan, Taylor, Peake, Houghton and

[illegible]

Yangtze drainage and was present coastwise from Shanghai to Hongkong These later workers found *Oncomelania hupensis* to be the molluscan host in the Yangtze Valley and *Katayama nosophora* along the southeast coast.

Tubangui (1932) incriminated *Oncomelania quadrasi* (syn. *Schistosomophora hydrobiopsis*) as the intermediate host of the etiological agent of human schistosomiasis japonica in the Philippines, while he and other more recent investigators have studied the distribution of the infection in these islands. Brug and Tesch (1937) and Bonne *et al* (1942) have demonstrated autochthonous infection in a small area in Central Celebes

As a result of exposure of approximately 2,000 American and 500 Australian troops to schistosomiasis japonica on Leyte, Philippine Islands between October 20, 1944 and May, 1945 opportunity was provided for extensive studies on the epidemiology, pathogenesis, symptomatology, diagnosis, treatment and experimental control of the disease. Clinical investigation of the early stage materially enhanced the knowledge previously obtained from relatively isolated observations on this phase of the disease. Some of the more important papers by American investigators of this epidemic and its sequelae are cited in the bibliography. Reference should also be made to the report of Dakin and Connellan (1947) on the outbreak in the Royal Australian Air Force

The cercaria which Sewell (1919) recovered from *Indoplanorbis exustus* and *Lymnæa amygdalum* in Calcutta, as well as the one described by Porter (1930) from *Lymnæa natalensis* in Durban, Natal, closely resemble that of *S japonicum*, but the actual identity of these cercariæ has never been adequately demonstrated

Geographical Distribution.—Schistosomiasis japonica is confined to the Far East and its distribution is coextensive with that of the small amphibi- [illegible] sely related genus *Oncomelania.* [illegible] hina, Formosa, the Philippines [illegible]

In Japan the disease is confined to five small foci, separate from one another, lying in widened valleys of coastal rivers Four of these endemic areas are on the island of Honshu, one northeast of Tokyo, two near Mt. Fuji and one near Okayama; the other is in the northern part of Kyushu Altogether these districts amount to only a few hundred square miles, and involve less than 100,000 people The recent survey of Wright *et al.* (1947) reveals that the incidence of the disease in Japan varies from less than one per cent in the Tone River area to more than 50 per cent in the Kofu area

In Formosa an infected area is situated at Shinchiku near the northwest coast of the island As far as is known man is not infected in this latter d[illegible] mammals [illegible] e on five of the islands, Luzon, M[illegible] One endemic focus has recently been discovered on the southern tip of Luzon (Pesigan, 1947) On Mindoro there is a moderately extensive area of endemicity on the northeast coast There are numerous coastal and inland foci on Samar The Leyte valley constitutes a highly endemic region, with an incidence among older children as high as 80 or 90 per cent in some localities (Bang *et al*, 1945) On Mindanao there are several endemic areas, including the Surigao peninsula,

Bandeira and Pires (1940) reported a presumably autochthonous case of Oriental schistosomiasis among Japanese colonists in the Matto Grosso, Brazil. Nevertheless, there is no proof that it has become established in the Western Hemisphere.

Stoll (1947) has estimated the total incidence of schistosomiasis japonica to be 46 million, all in eastern Asia.

Structure and Life Cycle.—The adult worms of this species were carefully described by Katsurada (1904) in his original investigation of the species. The male is the larger, more robust and the female the more slender and longer (Fig. 43). In typical infections the males and females are about equal in number and the females are usually situated in the gynecophoral (sex) canal of the male, which extends from a plane just behind the ventral sucker to the posterior extremity. (See figure.) Both males and females lack the tuberculated integument found in *S. hæmatobium* and *S. mansoni*. The suckers lie close together at the anterior end. The ventral sucker in both sexes is like a shallow cup on a short broad base. The esophagus is surrounded by clusters of glands (Fig. 44). The intestine bifurcates just in front of the ventral sucker, the ceca continuing posteriad to the last fourth or fifth of the body before reuniting.

The males measure from 12 to 20 mm. in length by 0.50 to 0.55 mm. in greatest diameter. Their integument is grossly smooth, but is actually covered with minute acuminate spines, which are most conspicuous in the regions of the suckers and of the gynecophoral canal. The testes are characteristically seven in number, although at times they may consist of only six. They lie side by side in a single column (Fig. 44). Each is provided with a short vas efferens, which joins its mates to form a common vas deferens, the latter enlarging into a seminal vesicle before opening to the exterior through the genital pore. There is no muscular cirrus organ.

The female attains a length of 26 mm. and has an average diameter of about 0.3 mm. The integument is non-tuberculate but is provided throughout with minute acuminate spines. The ovary is situated somewhat behind the middle of the body in front of the union of the intestinal ceca. Posterior to the ovary are the vitelline glands, which occupy most of the posterior fourth of the body. Emerging from the posterior end of the ovary is an oviduct, which bends abruptly forwards and, running parallel to the vitelline duct, proceeds to the oötype. There is a seminal receptacle lying coiled to the right at the posterior end of the ovary; this store-house for spermatozoa joins the oviduct near the origin of this duct. Fertilization may, therefore, take place before the naked egg cells reach the oötype. The oötype lies just in front of the midplane of the body. It is surrounded by Mehlis' gland, which opens into its lumen, and is provided anteriorly with a sphincter which separates it from the uterus. The uterine tube is long, extending from the ootype to the genital pore immediately behind the ventral sucker. It may contain 50 or more eggs. The eggs in the proximal end are almost hyaline, while those near the genital pore are a pale yellow. The more mature uterine eggs are biconvex and regularly oval in outline, except that there is typically a shallow depression on one side near one end, from which there extends a short recurved hook or abbreviated spine. The eggs which are ready for laying are still immature; they measure approximately 67 by 50 μ.

When the female worms are ready to lay their eggs they extend the anterior part of their bodies considerably in front of the males into the smaller venules of the submucosa (see Fig. 52), or even into the mucosa (*Faust and Meleney, 1924) but they apparently do not leave the gynecophoral* canal of the males. Here large numbers of eggs are deposited into the capillaries of the mucosa or submucosa, which become enlarged and congested. The eggs are thus deposited very close to the lumen of the intestine, where, by the slightest pressure, or by digestion of the intestinal epithelium resulting from lytic secretions of the maturing miracidia oözing out through minute pores in the egg shells, they are discharged into the lumen of the gut. The first eggs which are laid by the female worms pass through into the intestinal lumen almost immediately after deposition and are consequently still immature. As egg-laying proceeds and the intestinal

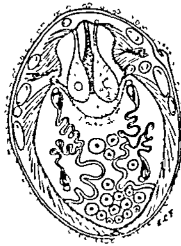


FIG. 15.—Mature egg of *Schistosoma japonicum*, with enclosed miracidium. The blood cells adherent to the shell are characteristic. × 60. (Original.)

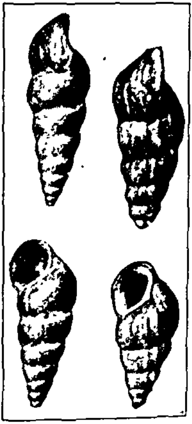
FIG. 16. Miracidium of *Schistosoma japonicum*. × 550. Lettering as in Fig. 23. (After Faust and Meleney, Am. Jour. of Hygiene.)

wall becomes more and more thickened, the interval between deposition and extrusion becomes longer and longer, so that all stages of maturity of the eggs may be found in the tissues, while in chronic cases calcified and otherwise devitalized eggs may accumulate. As the route into the lumen of the gut becomes more and more obstructed, eggs are more commonly swept along in the blood stream into the liver. Vogel (1942) has provided a detailed description of the types of *S. japonicum* eggs recovered from tissues of experimental hosts and Faust (1946) has supplemented this with a description of the great variety of these eggs which may be found in the patients' stools.

The eggs extruded into the intestinal lumen (Fig. 15) are voided with the feces. They measure from 70 to 100 μ in length by 50 to 65 μ in breadth. Defecation in endemic areas may occasionally be promiscuous, but the stool is more frequently saved for manurial purposes. Night-soil is usually conserved in a liquid state in reservoirs which are situated on the banks of terminal or irrigation canals, where ample opportunity is afforded for the

eggs to reach the water, thus providing conditions favorable for hatching. When the temperature is mild hatching of mature viable eggs will occur within a few hours. In cooler climates during the winter months, such as obtain in Central China and Japan, the eggs may over-winter in a viable state and hatch the following spring at the time the molluscan host becomes reactivated (Faust, 1917). The shell membrane splits along the line of least resistance, allowing the miracidium (Fig. 46) to escape. On emerging from the shell on the substratum the larva breaks out of its embryonic membrane, then begins to swim energetically in the water, the forward movement causing it to elongate somewhat. Like the miracidia of *S. hæmatobium* and *S. mansoni* it is provided with a ciliated epithelium, which is interrupted only

Fig. 47



A B

Fig. 48

Fig. 47 —Habitat of *Oncomelania (Katayama) nosophora*, the molluscan host of *Schistosoma japonicum* in Japan (Original photograph.)

Fig. 48 —Molluscan hosts of *Schistosoma japonicum*. *A*, *Oncomelania hupensis*; *B*, *O* (*Katayama*) *nosophora*. × 5. (After Faust and Meleney, Am. Jour. of Hygiene)

at the very anterior end, at the openings of the lateral secretory gland ducts and at the openings of the two excretory ducts. Internally the miracidium of *S. japonicum* is provided at its head end with a primitive gut (*pg*), a pair of penetration glands (sg_1), packed with granular oxyphilic material and opening to the sides of the gut, and paired clusters of minute penetration glands (sg_2) of a basophilic reaction lying immediately posterior to the gut and having bundles of capillary ducts (*sgd*) opening through minute pores at the anterior-lateral margins. A central neural mass (*n*), with longitudinal extensions, is situated underneath the basophilic secretory glands. There are two pairs of flame-cells (*fc*) with ducts (*ct*) uniting on either side into a single collecting tubule, which opens

through pores on the postero-lateral margin (*cp*). Germ balls are proliferated from the posteriorly disposed germinal epithelium into the lumen of the miracidium, which serves as a brood cavity.

After swimming about for a short time in the deeper strata of water the miracidia of *S. japonicum* rise to within 2 or 3 cm of the surface, where they continue to swim about for twenty-four to thirty-two hours It is in this top stratum that the appropriate snail is most likely to be found, particularly at the time when the water begins to rise to the level of those snails which are attached to grass and weeds on the banks of canals and irrigation ditches (Fig. 47).

The molluscan intermediate hosts of the infection in Japan and along the coast of China from Shanghai to Canton, where the water comes from coastal mountain streams, as well as in Szechuan Province (upper Yangtze tributaries) is *Oncomelania* (*Katayama*) *nosophora* Robson (Fig. 48 *A*), throughout the central and lower Yangtze Valley, where the water is more loaded with salts and débris, the host is *Oncomelania hupensis* Gredler (Fig. 48 *B*); in the endemic foci of Yunnan Province, southwestern China, it is believed to be *O.* (*Schistosomophora*) *robertsoni;* in Formosa it is *O.* (*Katayama*) *formosana* (Pilsbry and Hirasé); and on the Islands of Leyte, Samar, Luzon, Mindoro and Mindanao (Philippines), it is *Oncomelania* (*Schistosomorphora*) *quadrasi;* (syn. *Blanfordia quadrasi, Schistosomorphora hydrobiopsis*) *O mœllendorfi*, *O. tangi* and *O. yaoi*, all from China, have been found naturally infected or are known to be susceptible to infection in the laboratory. The molluscan host in the Lake Lindoe area of Celebes is unknown For detailed studies on the ecology of *O. quadrasi* on Leyte the reader is referred to McMullen (1947).

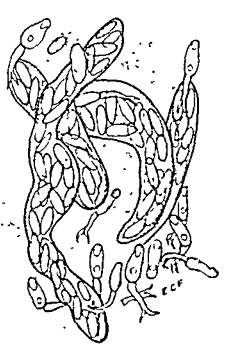


Fig. 49 Second generation sporocysts, with escaping cercariae of *Schistosoma japonicum* dissected out of infected *Oncomelania quadrasi* molluscan intermediate host in the Philippines × ca 100 (Original)

An apparently acceptable molluscan host for *S. japonicum*, *Pomatiopsis lapidaria*, has a wide distribution in the United States. Abbott (1948) places the genus in the same family and sub-family as the natural hosts of this blood fluke in the Orient. Stunkard (1946) obtained partial development in *P. lapidaria* and Berry and Rue (1948) have more recently demonstrated completion of the molluscan phase of the life cycle in experimentally infected, laboratory-bred snails of this species

On coming in contact with the appropriate snail the miracidium of *S japonicum* attacks and penetrates the soft parts of the mollusc

It may either enter the gill filaments and soon reach the blood stream, from whence it is carried to the lymph channels, or it may invade the soft mesenchymatous tissues of the head or foot. In the latter event it digests the host tissue to form an artificial lymph channel, which soon extends to the true peri-intestinal lymph sinuses. Meanwhile the ciliated epithelium is sloughed off, and the miracidium is transformed into a sporocyst, which migrates towards the lymph spaces bathing the digestive gland, where second generation sporocysts (Fig. 49) develop within the parent sporocysts, erupt into the free lymph spaces surrounding the digestive gland, and, in turn, produce internally the fork-tailed cercariæ. These latter, on maturing, are crowded within the thin-walled second generation sporocysts which pack the lymph spaces. On reaching complete maturity the cercariæ work their way out of the second generation sporocysts and are ready to emerge from the snail. This occurs only in case the snails are in the water. Thus, snails which have bored into the earth during the period of hibernation, those attached to grass above the water line or those in cracks of dry earth may be heavily infected but are not freed of their parasitic progeny until they fall into water or the water level rises to meet them, whereupon within a few hours swarms of cercariæ erupt from the host tissues and rise to the surface of the water, where they may attach themselves by their ventral suckers or again sink to the bottom of the water. It is this brood of cercariæ lying just under the surface film in quiet shallow water which is *probably responsible for the* greater part of the infection acquired by persons wading in the infested water.

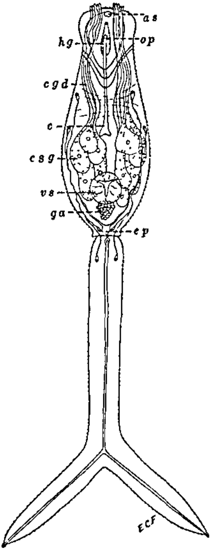


Fig 50 —Cercaria of *Schistosoma japonicum.* × 340 Lettering as in Fig 25. (Original)

The free-swimming larva (Fig. 50) is a characteristic schistosome cercaria, with a forked tail and with the entire integument provided with minute spines. The body proper measures 100 to 160 μ in length by 40 to 66 μ in transverse diameter. The tail trunk averages from 140 to 160 μ in length by 20 to 35 μ in cross section, and the furcæ from 50 to 75 μ in length. The anterior sucker (*as*) lies in front of the oral aperture (*op*). On its dorsal side there is a head gland (*hg*) opening into its blind inner aspect. A capillary esophageal tube leads into an enlarged, bilobed cecum (*c*), which ends blindly near the middle of the body. The ventral sucker (*vs*) is

situated in the posterior fourth of the body. It is small but very muscular Just behind it there is a clump of genital cells (*ga*). The excretory system is identical with that of the other human schistosome cercariæ, consisting of two pairs of flame-cells on either side of the mid-line, the posteriormost cell residing in the proximal part of the tail. The collecting tubules enter the bladder from its anterolateral aspects. The bladder has a minute dorsally situated excretory pore A collecting tubule also extends from the posterior face of the bladder into the tail, bifurcating as it reaches the caudal furcæ and opening at the end of each furca through a minute pore. The penetration glands consist of five pairs of cells having granular contents, situated between the fork of the cecum and the posterior plane of the acetabulum. Tang (1938) has found that the two anterior pairs of glands are oxyphilic and contain relatively coarse granules, while the three posterior pairs are basophilic and contain finer granules The anterior glands stain blue with alizarin dye and the posterior glands a strawberry red with lithium carmine. With intra-vital water-soluble alizarin sodium sulfonate the anterior glands stain pink and the posterior glands remain unstained.

On coming in contact with the exposed skin of a mammal, the cercaria attaches itself and attempts to penetrate the skin This process is materially aided if the water-film containing the cercariæ on the surface of the skin begins to dry. All mammals which frequent "infected water" in infected areas appear to be susceptible to infection Before attempting invasion or during the process the tail is discarded *After a period of* twenty to twenty-four hours the cercariæ have digested their way through the skin, utilizing the lytic ferments elaborated in the penetration glands and poured out through the duct openings at the head end of the organism Thus they reach the bloodvessels or lymph nodes, from whence they pass *directly to the lungs In ordinary infections the larvæ slowly squeeze* through the capillaries of the lungs into the left side of the heart and out into the systemic circulation, but in overwhelmingly heavy invasions the larvæ may break through the capillaries into the lung tissue and at times into the pleural cavity Only in such an event is there any possibility of *the larvæ attempting to invade the abdominal cavity through the diaphragm, and such an attempt* is bound to end in failure, since the contents of the glands (the means of penetration) have been previously exhausted and are not replenished From the aorta the majority of the schistosomulæ in the systemic blood are directed into the vessels feeding the abdominal viscera Of this number only those entering the mesenteric arteries and passing through to the portal veins are capable of further development The remainder become lodged in small capillaries and are sooner or later absorbed By the eighth or ninth day after exposure to infection all of the young flukes destined to enter the portal system have arrived During the next few days they remain within the intra-hepatic portion of the system, feeding on blood cells and developing rapidly *As they begin to mature* they migrate against the blood stream into the mesenteric radicles, where they complete their development and where mating even of the premature worms takes place Vogel (1942) has found that unfertilized eggs are laid as early as the twenty-fifth or twenty-sixth day after skin exposure and

that the earliest fertilized eggs may be recovered one day later, but that a minimum of nine more days is required before the eggs contain mature miracidia. At the end of about five weeks after the entry of the cercariæ into the body mature and maturing eggs begin to appear in the stools.

Epidemiology.—This is not essentially different from that of schistosomiasis mansoni. The water in which the snails breed is polluted by human feces. In the Orient the contamination of water frequently results from human night-soil used for fertilization of crops, or from latrines built over shallow, rather stagnant backwater which is periodically washed out into currents of fresh water by heavy rains. Sanitary buckets and commodes are rinsed out in the canals, earthen jars containing human night-soil pollute the banks of canals and night-soil boats contaminate the water.

Fig. 51.—Case of giant urticaria with fever in American youth, six weeks after swimming in infected water in Central China (Photograph by Dr. H. E. Meleney)

Likewise, to a lesser degree, dogs, cats, pigs, horses, cattle and water buffaloes, likewise semi-domestic rodents, infected with *S. japonicum*, contribute to the infestation in the water. Once the cercariæ have developed in the appropriate snails and have been discharged into the water, human infection results from wading in the shallow water along the banks of the canals and irrigation ditches, or in the rice nursery beds and paddies, bathing in the water and washing clothes on the banks of streams. On Leyte during military operations late in 1944 there was evidence that bathing in salt water and then rinsing off in fresh water constituted adequate exposure (Sullivan and Ferguson, 1946).

Schistosomiasis japonica may be contracted as a prenatal infection. In 1916 Narabayashi reported eggs of this infection from the stools of three newly-born babies, whose mothers worked in the rice fields in endemic areas in Japan. More recently Hovard (1933) reported infection in a fourteen-day-old infant of an Asiatic family traveling in British Guiana.

Pathological and Clinical Aspects of Schistosomiasis Japonica.—Schistosomiasis japonica or Oriental intestinal schistosomiasis has been known under various names including those of a geographical nature (Katayama

disease, Yangtze Valley fever, Hankow fever, Kiukiang fever) and those of symptomatic significance (urticarial fever and neurangiotic edema). In the lesions produced and in its symptomatology this disease closely resembles schistosomiasis *mansoni*, although the symptoms frequently appear earlier in Oriental schistosomiasis and are usually much more severe for the same amount of exposure. Both the pathological anatomy and symptoms of the disease may be separated into the three stages which have been described in schistosomiasis hæmatobia and schistosomiasis mansoni, namely, (1) the incubation period, (2) the period of egg deposition and extrusion and (3) the period of tissue proliferation and repair (Faust, 1946).

The Incubation Period.—The symptoms during the first stage of the disease are similar to those of the other schistosomiases, although there appears to be evidence that in some cases, at least, urticarial rash, unaccompanied by febrile reaction, may develop as early as five days after exposure to infection. This is about the time when aberrant larvæ become lodged in small bloodvessels, and so may be responsible for the reaction. There are abundant data, however, to show that the onset of symptoms, consisting of discomfort in the epigastric region, an enlarged, tender liver which can usually be palpated under the right costal margin, pains in the back, groin, legs or along nerve tracts, with afternoon fever (38° to 39.5° C.), often

and voice sounds and moist râles. At times these signs and symptoms are accompanied by an intense urticaria (Fig. 51) with localized edema, involving the subcutaneous tissue. The wheals vary in size from a few millimeters to several centimeters in diameter, are raised, firm, white in color, round or irregular in contour and are surrounded by a broad red areola. They appear on all parts of the body, including the mucous membranes, and are attended by intense itching of the affected parts. This condition may last from one day to two weeks There is usually a leukocytosis at this stage and a more or less intense eosinophilia, at times as high as 90 per cent. Blood is not present in the feces at this period except in very heavy infections.

Natives in endemic foci are usually exposed to infection time and again, so that infected individuals commonly display several progressive stages of the disease at one time One epidemic is known in which 40 native school boys, bathing in an infected pool at Anking, Anhwei Province, China, all acquired the infection, the onset

month after exposure. Likewise, during th

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patients experienced the characteristic urticarial rash, malaise and exhaustion, fever and sweats, with leukocytosis and eosinophilia during the prodromal period of the disease (Kastein, 1932). From late October, 1944 through the spring of 1945 there were many hundreds of military patients on Leyte, P. I who were observed by skilled physicians during the end of

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the incubation period and subsequently. Some patients manifested symptoms of profound intoxication, others were moderately sick and still others were essentially asymptomatic during the incubation and prodromal stages. There appears to be little doubt, therefore, on the basis of the cases observed, that this stage of the infection is ordinarily attended by the classical symptoms of schistosomiasis toxemia.

As far as is known, the lesions produced by *Schistosoma japonicum* during the stage of migration and maturation of the parasite have been studied histologically only in experimental animals. They consist in (1) definite skin eruption associated with the penetration of the cercaria, which is most conspicuous from the twenty-fourth to the thirty-sixth hour and disappears after eighty-four hours (according to Watarai, 1936, there is no local cellular reaction following invasion of the cercaria into the skin); (2) lesions in the lungs during passage of the parasites through these organs and in intense infections having the gross appearance of diffuse hemorrhagic pneumonia even up to the fourteenth day; (3) lesions in the stomach,

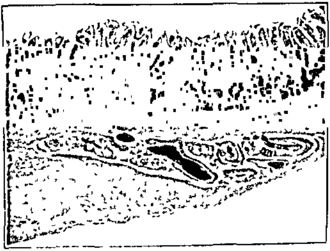

FIG 52.—Adult males and females of *Schistosoma japonicum* in veins of the submucosa, females depositing eggs which are filtering through the mucosa into the intestinal lumen (Enlarged, from Faust and Meleney, Am. Jour of Hygiene)

kidney and other organs due to escape of the schistosomula from the blood-vessels into the tissues, and (4) hemorrhagic congestion in the liver, spleen and duodenum in heavy infections during the period of maturation of the parasites.

The Period of Egg Deposition and Extrusion.—The second period of the disease, that of egg deposition and extrusion from the mesenteric-portal vessels into the tissues, immediately succeeds the first stage. It is ushered in by symptoms of dysentery, with eggs of the parasite in the stools. This is accompanied by daily fever and epigastric pain, with tenderness over this area, loss of appetite and weight. The liver is somewhat enlarged and the spleen may be palpable. After a period of three to ten week's rest the patient, if untreated, slowly regains his strength, his temperature becomes normal, and he may return to work, although special exertion commonly brings on a recurrence of the dysentery, and the patient remains underweight. The blood picture is that of a secondary anemia, with a low hemo-

globin index and at times a leukopenia, usually with a marked reduction in the number of eosinophils.

The primary pathological process responsible for the clinical picture of this stage is the development of multiple lesions around the eggs which have been extruded into the intestinal wall, mesenteric lymph nodes and liver tissue. Hoeppli (1932) has demonstrated the actual discharge of secretions through the shells of eggs lodged in the tissues, and has suggested that such discharges probably constitute one of the provocative factors in the early cellular infiltration around the eggs. In the intestine the worms

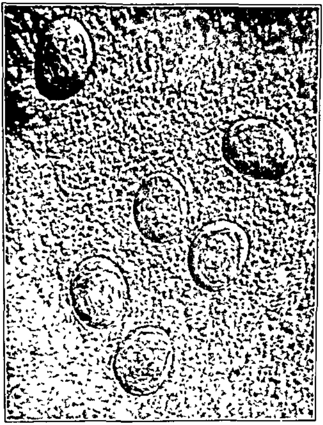

FIG. 53.—Eggs of *Schistosoma japonicum* in bloody mucous exudate from case of acute schistosomiasis japonica dysentery × 200 (From Faust and Meleney, Am Jour. of Hygiene.)

may be found in the vessels of the submucosa (Fig. 52) or even the mucosa, and the eggs are at times deposited still further distally in the capillaries, so that they are massed into radiating rows in the stroma of the mucosa from the central point in the submucosa, some being situated quite close to the intestinal lumen. The least pressure causes a rupture of the intestinal epithelium and the nearest eggs are extruded into the lumen of the intestine along with blood and mucus (Fig. 53). Congestion first appears in the mucosa and submucosa but later the serous surface is also involved. Microscopically these lesions center around eggs which come to be surrounded by concentric layers of white cells, conspicuous among which are eosinophils

Thus the typical schistosomiasis pseudo-abscess is formed. It seldom, if ever, undergoes necrosis, but frequently breaks through into the lumen of the gut, discharging its contents through small openings between intestinal glands. Repair of injured tissue sets in rapidly, with formation of granulation and scar tissue (Fig. 54). Coincident with this process is the proliferation of glandular epithelium along the periphery of the abscess, so that at times it entirely surrounds the abscess cavity.

Many of the eggs discharged by the female worm are carried by the blood stream into the liver, where they break through the walls of the vessels into the tissue, there to produce similar schistosomiasis abscesses. These may enlarge, with a degeneration of the more centrally disposed cells and without fibrous-tissue formation on the periphery, or they may become

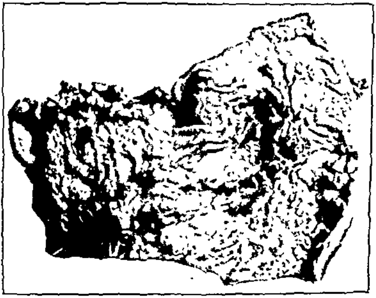

FIG. 54.—Mucous surface of the colon in a case of human schistosomiasis japonica, showing papillomata. (From Faust and Meleney, Am. Jour. of Hygiene.)

walled off on their periphery by fibroblasts with a definite attempt to encapsulate the egg (Fig. 55). Later on, foreign-body giant cells may develop within the pseudo-tubercles. Along with these changes is the engulfing of small particles of hematin pigment, which had been discharged from the alimentary canal of the parent worms after their digestion of the host's red blood cells, phagocytosed by the endothelial cells of the blood capillaries in the liver parenchyma, by the large phagocytic cells in the portal spaces, and by similar cells in the organizing portion of the pseudo-tubercles. Thus, fibrosis of the liver gets under way while the organ is still enlarged as a result of inflammatory processes. This combined damage is due to the presence of an increasing number of eggs which have infiltrated out of the portal venules into the tissues, as well as from the toxic metabolites of the parent worms situated in the mesenteric venules.

Congestion and marked enlargement of the spleen, with increase of the fibrous reticulum, and enlargement of the mesenteric lymph nodes, with loss of active lymphoid tissue, are also conspicuous features of this stage of the disease.

The Stage of Tissue Proliferation and Repair.—The third period of the infection, that of tissue proliferation and repair, is characterized conspicuously by cirrhosis of the liver Since natives in endemic areas are constantly exposed to reinfection, the picture of this stage is usually combined with that of the second stage of the disease However, Japanese investigators have conducted experiments suggesting that partial immunity may be acquired to subsequent infection by an initial host tissue reaction to the worms. In young patients retardation of development, both physical and sexual, is common. On palpation, the abdomen usually reveals an enlargement of liver or spleen or of both organs The surface of the liver is hard and is covered with myriads of minute nodules about the size of a millet seed (*i. e.*, the pseudo-tubercles around eggs as centers). The

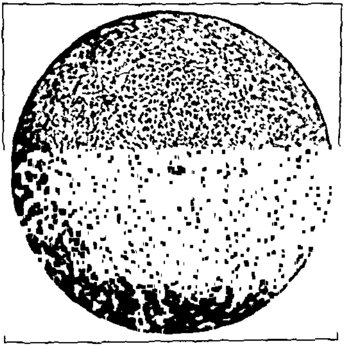

FIG 55—Organizing abscess or pseudotubercle around egg of *Schistosoma japonicum* in liver tissue (From Faust and Meleney, Am Jour of Hygiene)

mesentery and omentum are frequently thickened, binding down the colon in a firm mass, so as to present an enlargement in the upper abdomen and another in the lower quadrants, with an intermediate constriction (Fig 56). Weakness and extreme pallor of the skin are general and dyspnea on light exertion is usually present. Emaciation is often extreme Ascites is at times relatively slight but is more often pronounced. Dilatation of the veins of the abdomen and thorax is often marked (Fig. 57). The thorax is cone-shaped and the thoracic viscera are frequently pressed upward due to increase of the abdominal contents. Hepatic facies is usually pronounced. The blood-pressure is often subnormal, and the daily temperature may vary within wide limits

The red blood cells are markedly reduced; the hemoglobin per cent and

the color index are both low. Eosinophilia is frequently less pronounced than during the earlier stages of the disease. Precipitation, intradermal reaction and complement-fixation tests are usually positive at this stage, indicating an increase in the blood serum euglobulin and of specific antibodies.

The feces frequently consist of poorly digested food, with occasional flecks of blood and mucus, while eggs of *Schistosoma japonicum* are commonly distributed throughout the entire fecal mass. At times they may be

FIG 56.—Case of schistosomiasis japonica Second stage, showing enlarged upper and lower portions of abdomen and constricted middle region. (From Faust and Meleney, Am Jour of Hygiene)

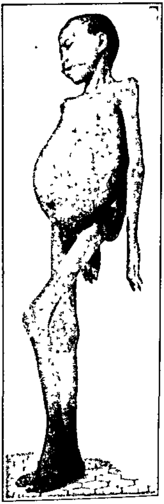

FIG. 57 —Advanced clinical schistosomiasis japonica, with marked ascites, prominent abdominal veins, emaciation, and hepatic facies. (Photograph by Dr. J H Foster)

so few in number as to be found with difficulty by ordinary smear examination; or the majority of the eggs may be so abnormal in appearance as to be overlooked or misinterpreted by the diagnostician. The development of ascites is accompanied by a diminution of urine output, but otherwise the urine is usually normal.

Patients with progressive hepatic cirrhosis may go on for many years and only present themselves for treatment in the last stages of the disease.

In light infections patients may live for fifteen years or more, although the pathological processes at work during this time undoubtedly shorten the expectation of life and lower the resistance of the patient to other infections. Moreover, in approximately 12 per cent of schistosomiasis japonica patients the infiltration of eggs of the parasite in the myocardium may cause a complication of hypertension. In repeated infections, there is a consistent decrease in liver function, with the development of marked ascites, which can be only temporarily relieved by paracentesis. The patient gradually goes into a decline and may die of exhaustion, or bronchopneumonia, appendicitis or malaria may hasten the end.

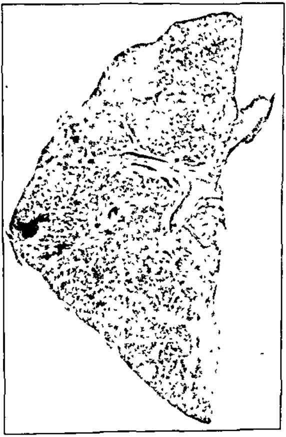

FIG. 58.—Hepatic cirrhosis in human case of schistosomiasis japonica × ½. (From Faust and Meleney, Am. Jour. of Hygiene.)

The essential pathological picture of this third period is one of great thickening of the intestinal wall, due to scar formation in all layers, development of papillomata of the mucosal surface of the gut, shortening and thickening of the mesentery, thrombosis of the mesenteric and portal ... (Fig. 58) brought about (1) by

... portal

... secre-

tions from eggs which are continuously escaping into the portal blood and are being deposited into the tissues. This is the same picture as that

described by Symmers for *S. mansoni* infection under the name of "clay pipestem cirrhosis." In addition, the spleen is typically hypertrophied, with a marked increase in the fibrous reticulum and corresponding decrease in the functional cells.

Ectopic Schistosomiasis Japonica.—The earlier Japanese pathological literature referred occasionally to Jacksonian epilepsy resulting from nests of *S. japonicum* eggs in the brain (Yamagiwa, 1889; Shimamura and Tsunoda, 1905). Isolated clinical and pathological reports of ectopic schistosomiasis japonica have likewise been made in China and the Philippines. As of 1947 (Faust, 1948) at least 49 cases were known, compared with 21 for vesical schistosomiasis and 12 for Manson's schistosomiasis. Of the 49, 44 involved the brain, one the spinal cord, two the heart, and three the skin and peripheral blood vessels. More than half of the total, or 28 cases, resulted from infections acquired by American troops in the Philippines between 1942 and 1945, mostly in the winter of 1944–1945. In some patients symptoms developed during the acute stage of the disease and in others as a sequela, at times without a previous history of abdominal symptoms (Carroll, 1946).

Diagnosis.—There are few clinical landmarks during the incubation period, prodromal stage or acute stage in schistosomiasis japonica which are in themselves pathognomonic of the disease. However, a history of exposure to raw fresh water in an endemic area, together with extreme toxemia, allergic manifestations, late afternoon fever, abdominal distress, enlarged, tender liver and rising eosinophilia, are definitely suggestive. During the period of incubation the disease requires differentiation from typhoid fever, while the urticaria must be distinguished from food toxemia and angioneurotic edema. The enlarging, tender liver might be regarded as due to infectious hepatitis, relapsing fever or even amebic hepatitis. The dysenteric symptoms of the period of egg extrusion must be clearly differentiated from those of bacillary or amebic dysentery, intestinal tuberculosis, hookworm disease and typhoid fever. Concentrated in the wall of the appendix, the eggs frequently set up cellular reactions suggestive of acute or subacute appendicitis (Ozawa, 1928). The stage of liver cirrhosis may be confused with Lænnec's cirrhosis or even syphilitic cirrhosis or tuberculous peritonitis with ascites. Splenomegaly of schistosomiasis japonica may mimic that of malaria or other diseases involving the hematopoietic system Pronounced eosinophilia favors a diagnosis of schistosomiasis japonica in persons who have lived in endemic areas, while the recovery of *Schistosoma japonicum* eggs from the stool is definitely diagnostic.

Laboratory Diagnosis.—The relative efficiencies of the direct fecal film, concentration of the stool by different methods, hatching of miracidia, rectal aspirate or biopsy material, as well as immunological and serological diagnosis, have been given critical trial in recent years Summary information is provided here but the reader is referred to Section VII for details of technic

Direct fecal films, including representative samplings of mucus and of feces, should always be made first and in a fair number of *S. japonicum* infections will provide positive diagnosis by demonstration of the eggs. This method is particularly valuable in active infections with considerable

amounts of blood-streaked mucus in the stools. Nests of eggs will often be found in the mucus. When eggs are relatively few, as in more chronic infections or those which are apparently symptomless, concentration technics are needed. If 5 to 10 Gm or more of feces are available, *sedimentation*, using 0.5 per cent glycerin in water as the sedimenting medium, is most practical. This is the most satisfactory method for old chronic infections and for post-treatment stool examination. If only one to two Gm. of stool are available the *HCl Acid-Sodium Sulfate-Triton-ether concentration technic* should be employed. The *hatching technic* (Faust and Meleney, 1924; Andrews, 1935) is preferred by some diagnosticians.

In schistosomiasis japonica, as in schistosomiasis mansoni, there are occasions when stool examination is consistently negative but when *aspirates or biopsies of rectal mucosa* yield positive diagnosis.

Immunological and serological tests, including the intradermal reaction and complement fixation with schistosome antigen, and the non-specific precipitation test of Sia and Wu or the aldehyde (formal gel) test, occur during the chronic stage in a majority of cases but can not be depended on in earlier infections (Wright *et al.*, 1946).

Because of the increasing damage caused by a continuing infection of schistosomiasis japonica, it is important to obtain specific diagnosis as early as possible. The eggs obtained for diagnosis from the stool or rectum are by no means always typical; they may be immature, degenerate, calcified or surrounded by one or more layers of host's tissue (Faust, 1946). These [illegible] vegetable cells, while, on the other hand, [illegible] may consider undigested vegetable cells as atypical eggs of *S. japonicum*. Finally, the possibility of the development of ectopic foci of the disease demonstrates the need for early specific diagnosis.

Therapeusis.—Potassium antimony tartrate (tartar emetic) or sodium antimony tartrate is specific for treatment of schistosomiasis japonica and its administration is usually indicated in early and moderately advanced cases. In late cases, where hepatic cirrhosis has proceeded beyond a period of functional recovery of the organ, administration of the drug probably does more harm than good.

Although the preparation with the sodium salt is somewhat better tolerated, it must be made up fresh each time it is used. In many dispensaries this is impractical. A careful clinical study of the efficacy of potassium antimony tartrate in schistosomiasis japonica was made in U. S. Army General Hospitals in 1945. It was found that no serious intolerance developed if the drug was administered by vein in a one-half per cent solution, according to the following time table: 1st day, 8 cc. (14.4 mg. Sb); 3rd day, 12 cc. (21.6 mg. Sb), 5th day, 16 cc. (28.8 mg. Sb), 7th day, 20 cc. (36 mg. Sb), 9th, 11th, 13th, 15th, 17th, 19th, 21st, 23rd, 25th, 27th and 29th days, 24 cc. each (43.2 mg. Sb), total, 320 cc. (0.576 Gm. Sb). This produced about 84 per cent cures.

Fuadin and other synthetic trivalent antimonials have much to recommend them, in that they are administered intramuscularly, require less careful administration and are less likely to produce bronchial irritation and liver reaction. However, even with a total treatment of 65 cc. (6.3

per cent solution), 20 cc. more than originally advocated and containing 0.566 Gm. Sb, the relapse rate is approximately 70 per cent as contrasted with 16 per cent for tartar emetic. Thus, fuadin is not the drug of choice in schistosomiasis japonica.

An entirely new chemotherapeutic, *Miracil* (1-methyl-4-diethylamino-ethylaminothioxanthone), which was synthesized by Mauss and was shown to be active against *S. mansoni* in mice by Kikuth and Gönnert, may in the future provide a satisfactory alternative for antimony preparations in all types of schistosomiasis (Wood, 1947), but this appears to be doubtful

Improvement is determined by the gradual improvement in the patient's condition, increased appetite and weight and the gradual diminution of the liver and spleen. Stool examination over the period shows a decrease in the number of eggs, their gradual degeneration and final disappearance The blood picture usually shows a coincident improvement, but eosinophilia and the presence of serum euglobulin may persist for some time after the treatment has been completed. Tartar emetic treatment is contraindicated in cardiac block, pneumonia, nephritis and advanced hepatic cirrhosis.

The value of emetine therapeusis in *Schistosoma japonicum* infection is doubtful.

Prognosis.—Good to fair in early cases, provided specific therapy is promptly administered; poor in all late and chronic patients with evidences of hepatic cirrhosis and fibrosis of the bowel wall. (For the same amount of infection, *i. e.*, the same number of worms, the prognosis is much less hopeful in schistosomiasis japonica than it is in schistosomiasis mansoni, due to the greater number of eggs produced by each female worm and a consequently greater number of pseudo-abscesses and pseudo-tubercles.)

Control.—The areas in the Far East where schistosomiasis japonica is endemic are practically all rice-growing districts. The disease is primarily confined to the rice farmers and river boatmen in these districts. The urban population is not seriously involved except in endemic areas in the Philippines, where women do the family laundering on the banks of infested streams and children play in the water. However, sportsmen, military forces and others who from time to time enter endemic foci, who wade or bathe in infected water, frequenty expose themselves to infection. In Japan domestic mammals and field mice (*Microtus montebelli*, *Apodemus speciosus*, *Mus molsimus*, etc.) serve as important reservoir hosts of the infection. In China Kuang Wu (1938) has found 12.6 per cent of 399 oxen and 18.7 per cent of 406 water buffaloes in the municipal abattoirs of Shanghai infected with *S. japonicum*. Dogs are also probably important as reservoir hosts in China In the Philippines dogs, pigs, water buffaloes (carabao) and rodents are common reservoirs and in the endemic focus in Celebes dogs and native deer are involved.

The infection is found only in the smaller irrigation canals and ditches, either in the rice fields or running up to the homes of villagers (Fig. 59) (China and Japan), or [illegible] washed into streams during tropical rains [illegible] lved in the infection are amphibious in the [illegible] of the quiet canals and ditches, where there is an abundant growth of weeds and grass. This usually occurs in stretches of loam, enriched with humus and fecal débris. The snails are never found in clayey soil or that on which no vegetation is

found. Along the canals running through the villages they are most frequently found near containers where night-soil is stored for ripening (China) or near latrines sitting over backwater (Philippines) From the ditches they become distributed into the rice fields at the time the water is treaded into the fields and develop most prolifically in the rice nursery plots which are heavily fertilized. They are definitely "dirty feeders"

In Japan it might be feasible to control the water supply over certain periods, but in China where each farmer is essentially a law unto himself as far as his crops are concerned, such control is out of the question Moreover, these snails are operculate and can withstand prolonged periods of desiccation, so that such attempts would produce no diminution in the number of snails. In at least one endemic area in Japan the application of unslaked lime on the banks of irrigation ditches and even in the rice fields resulted in almost complete destruction of the snails. In China, however, where the areas of infection are manifoldly more extensive, and where only sampling of snails from a few spots have been taken, the vast areas of infested waterways remain unsurveyed.

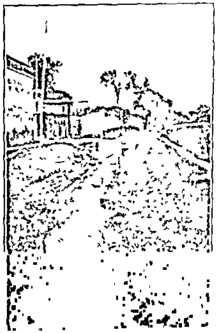

FIG 59—Terminal canal in schistosomiasis japonica endemic area near Soochow, China *Oncomelania hypensis* in vegetation along banks of canal (From Faust and Meleney, Am Jour of Hygiene)

It is obvious that control of the disease in China and the Philippines by attempts to destroy the molluscan hosts must be preceded by an exact survey of ground where the snails are likely to be found. Such a scheme is practically impossible as far as the whole area is concerned but appears to be feasible for certain important endemic foci, where the incidence of the disease is particularly heavy. The periodic application of lime along the banks of canals and ditches in such definitely delimited regions will prob- [illegible]ls, particularly if lime is mixed with [illegible]s in early spring, when the infected [illegible] Moreover, a dilution of quicklime, 1 part in 2000 parts of canal water, has been found to be sufficient to produce instantaneous death of the free-swimming cercariæ Burning the dry grass along the banks of canals during the winter season has also been suggested as a means of destroying the snail population. The addition of copper sulphate solution to canal water is not likely to be successful since the snails are most usually found on the grassy banks above the water surface, but it might prove to be valuable in eliminating the snails from rice plots, particularly rice nursery beds, and at the same time prevent further alkalinization of the soil.

There are several chemicals which in heavy doses will kill the snails and

their eggs. These include several di-nitro compounds, as di-nitro-cyclohexal-phenol and Dow K601 (McMullen, *et al.*, 1947). Application of these chemicals is justified only in military operations to protect troops, since it damages vegetation and is toxic to fishes and other animal life. Considerable protection is afforded by impregnating closely woven cotton trousers (uniform cloth) with dimethyl phthalate and tucking the lower ends of the trousers into the tops of well-made leather boots. Such impregnation survives several washings with laundry soap (Wright *et al.*, 1947). It is obvious that this type of protection is impractical for the average native population.

In China, where man is the important definitive host, it seems more likely that success in reduction of the disease may be attained by killing the *viable eggs before they reach the snails*. This may be accomplished by educating the farmer population in infected districts to conserve their night-soil long enough to sterilize the eggs through fermentation of the medium. In warm weather this occurs in two weeks or less; during the winter months it would require a longer time. Such a plan would not greatly reduce the fertilizer value of the night-soil. As has been previously suggested, therapeutic prophylaxis for the masses is out of the question in endemic areas of schistosomiasis japonica. In the Philippines, the construction of sanitary latrines, sterilization of water for household purposes by chlorination and the building of concrete platforms with simple laundry facilities would considerably reduce the danger of exposure. Thus it seems *most feasible to attempt to break the vicious cycle in endemic foci in* Japan, where the areas of infection are circumscribed and where man is only one of several important definitive hosts, by an antimolluscan campaign. In China, where the endemic areas are tremendous in size and mostly unsurveyed, and where man is the important definitive host, the problem of prevention and eradication seems most likely to be successful by centering the campaign on the destruction of the eggs of the parasite in the night-soil before it is distributed onto the fields. In the Philippines the problem is more strictly a domestic one. It could be solved by providing sanitary conveniences in the villages and educating the population as to the hazard of contact with raw water.

Schistosoma bovis (Sonsino, 1876) Blanchard, 1895.—(*The bovine blood fluke.*)

Synonyms. *Bilharzia bovis* Sonsino, 1876; *Bilharzia ovis* Cobbold, 1885; *Gynæcophorus crassus* (Sonsino, 1888) Stossich, 1892, *S. matthei* Veglia and Le Roux, 1929; *S. curassoni* Brumpt, 1931; *S. rodhaini* Brumpt, 1931; and *S. intercalatum* Fischer, 1934.

Schistosoma bovis was discovered by Sonsino in the portal vein of oxen and sheep in the Nile delta in April, 1876, and was later reported by Grassi and Rovelli (1888) in 75 per cent of the native sheep near Catania. It has since been reported from
[illegible], and, more rarely,
[illegible] otamia, the Malay
[illegible] the gray monkey
[illegible] mentally with cercariæ of this species, and also
[illegible] *pio porcarius*) He
[illegible] sia, who had eaten
a raw ox gut Cases of infection in man are apparently infrequent, although there

are reports of human infection in Natal, Southern Rhodesia and from the Stanleyville district of the Belgian Congo

The adult worms have been described in detail by Khalil (1924), Veglia and Le Roux (1929), Brumpt (1930) and Fischer (1934). The males vary in size from 15 to 22 mm. in length by 1 to 2 mm in thickness, while the females are 12 to 28 mm in length and are very slender. The integument of the male is tuberculate and is covered with minute spines. There are 3 to 6 testes, situated just behind the ventral sucker. The ovary is located at or behind the middle of the body The uterus contains a few to several dozen developing eggs, which are broadly spindle-shaped and may be distinguished from those of *S hæmatobium*, in that they are longer and narrower (170 by 45 μ), with a characteristic terminal spine (Fig 12, *4*) and almost always appear in the feces In South Africa and the Belgian Congo, *Physopsis africana* appears to be the appropriate intermediate host, in Kenya Colony, Dodeswell (1938) has infected *P. nasuta*, while in Corsica, Brumpt (1930) has incriminated *Bulinus contortus*. In Sardinia *B. contortus* var *sæprusanus* is involved, in Bagdad (Iraq), *B. truncatus*, and in Tunisia and Morocco, *B contortus* The cercaria is that of a typical blood fluke It measures 160 to 260 μ in length by 50 to 80 μ in diameter, has a tail trunk 180 to 280 μ long and 30 to 42 μ in section, and caudal furcæ 80 to 120 μ long There are two pairs of (anterior) oxyphilic and two pairs of (posterior) basophilic penetration glands. Infection with this parasite produces a typical intestinal schistosomiasis.

Schistosoma spindale Montgomery, 1906.

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which develop in *Indoplanorbis exustus* in the vicinity of Bombay Fairley and Mackie (1926) have investigated the pathological anatomy of this infection, their material showing marked thrombosis of the portal vessels and a periportal cirrhosis

The males of *S. spindale* range in size from 5 6 to 13 5 mm in length, and the females from 7 18 to 16 2 mm. The integument of the males may or may not be tuberculate, but is characteristically spinose. There are three to seven or more testes. The eggs (Fig. 12, *5*), which are very long, spindle-shaped objects with a terminal spine, are typically flattened or bowed on one side, and measure from

There is, how-
They are almost
e's experimental
material, worms were found in the iliac, azygos and renal veins and eggs in the bladder wall The cercariæ are narrower and have longer tail trunks than those of the other mammalian schistosome species They possess five pairs of penetration glands, two anterior oxyphilic and three posterior basophilic, and an accessory pair of flame-cells.

This infection in Indian cattle produces a nasal granuloma, from the lesions of which B
S spindale
Possible
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burg and
Zululand), where Annie Porter (1926) has experimentally incriminated *Planorbis pfeifferi* as the molluscan ho
part of Africa, in India an
has been found to be the
mnæa luteola and *L. acuminata*.
has found that the cercariæ of
The primary skin lesions are

not in themselves important, but the pruritus which they produce commonly causes scratching, with subsequent pyogenic infection of the sites. (*Vide infra, Cercaria dermatitis*).

Schistosoma incognitum Chandler, 1926.

Chandler (1926) found a non-operculate spined egg (*Schistosoma incognitum*) in supposedly human feces from the vicinity of Krishnagar, Bengal and from a Nepal
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Saunders (1934) believes that this schistosome is a natural parasite of the Indian pig, from the droppings of which animal in Madras he recovered presumably identical eggs. Bhalerao (1934) has described males of a blood fluke obtained from a Calcutta pig, which worms he identified as a variety of *S. japonicum*. These findings possibly all refer to one and the same species, but it is doubtful if they refer to the typical *S. japonicum*.

Schistosomatium douthitti (Cort, 1914) Price, 1931.

This mammalian schistosome is not described as a visceral parasite of man, although it develops in nature is several fur-bearing hosts in the Northern United States. Its molluscan hosts are a variety of fresh-water snails, including *Lymnæa reflexa, L. stagnalis* var. *appressa* and var. *perampla, Stagnicola exilis, S. palustris, S palustris* var. *elodes, S. emarginata-angulata, Physella parkeri* and *Physa gyrina elliptica* Penner (1941) suggests that *S. douthitti* may at times become a systemic parasite of man.

Cercaria Dermatitis.

Synonym.—Swimmer's itch.

Etiology.—In 1928 Cort showed that *Cercaria elvæ* Miller, 1923, a non-human schistosome larva developing in *Lymnæa stagnalis* var. *appressa*, and what was believed to be the same species of schistosome in *L.* (*Stagni-*

Lake region, *C. stagnicolæ*, developing in *Stagnicola emarginata-ang*... and *C. physellæ*, in *P.* (*Physella*) *parkeri* and *P. magnalacustris*. These two new species were probably part of the cercariæ described by Cort (1928) under the name *C. elvæ*. McMullen and Beaver (1945) demonstrated experimentally that these three types of cercariæ develop in experimental birds into species of the genus *Trichobilharzia, T. ocellata* (for *C. elvæ*), *T. stagnicolæ* (for *C. stagnicolæ*) and *T. physellæ* (for *C. physellæ*). Meanwhile Cort (1936) found that the cercaria of *Schistosomatium douthitti*, a mammalian blood fluke not known to mature in man, also produces dermatitis on contact with human skin. Szidat (1942) states that "*C.* ... closely
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that other non-human schistosome cercariae are the causes ... of dermatitis in man.

Geographical Distribution.—In addition to Douglas Lake other American lakes have been found to harbor snails discharging dermatitis-producing

cercariae, *viz.*, Michigan, additional lakes; Minnesota, several lakes (Christenson and Greene, 1928); Wisconsin, limited infection (Brackett, 1940); Oregon, vicinity of Portland, "*C. oregonensis*," probably *Trichobilharzia ocellata* (Macfarlane and Macy, 1946); Manitoba, Canada, *T. physellæ* (syn. *Pseudobilharzia querquedulae* McLeod, 1937) reported by Swales, 1936 and McLeod, 1937, and El Salvador, on lakes where Manitoba-banded ducks are caught during winter migration. Moreover cercaria dermatitis has been reported from Germany, France and Wales, caused by "*Cercaria ocellata*," and from the Federated Malay States (Buckley, 1938), where cercariae of *Schistosoma spindale* cause a pruritic dermatitis among paddy workers.

Pathogenesis and Symptomatology.—In susceptible individuals, as the water evaporates from the skin, a prickling sensation is experienced, followed by the rapid development of urticarial wheals. The condition subsides in about one-half hour, leaving only a few macules. Several hours

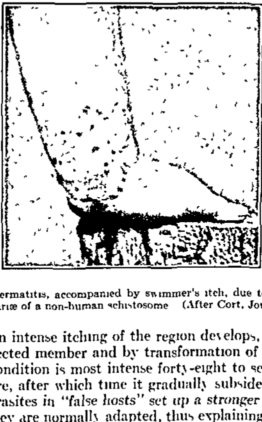

FIG 60—Cercaria dermatitis, accompanied by swimmer's itch, due to penetration of the human skin by cercariæ of a non-human schistosome (After Cort, Jour Am Med. Assn)

later, however, an intense itching of the region develops, accompanied by edema of the affected member and by transformation of the papules into pustules The condition is most intense forty-eight to seventy-two hours following exposure, after which time it gradually subsides. According to Vogel (1930), parasites in "false hosts" set up a stronger reaction than in hosts to which they are normally adapted, thus explaining the severe reactions observed in *Cercaria dermatitis*.

Diagnosis and Treatment.—Specific diagnosis can be made only in areas where careful parasitological surveys have demonstrated the presence of dermatitis-pr

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is palliative,

and prevent secondary infection

TABLE 1 — DIFFERENTIAL DIAGNOSIS OF THE THREE COMMON SPECIES OF HUMAN SCHISTOSOMES

	S. hæmatobium	*S. mansoni*	*S. japonicum*
ADULTS			
Male	*length* 10-15 mm *breadth* 0 8-1 0 mm *integument* finely tuberculated *testes* large, four	*length* 6 4-9 9 mm *breadth* 1 0-1 2 mm. *integument* grossly tuberculated *testes* small, six to nine	*length* 12-20 mm. *breadth* 0 5-0 55 mm. *integument* smooth except for minute spines on suckers and gynecophoral canal *testes* ovoid, compressed, seven, in one column
Female	*length* 20 mm *breadth* 0 25 mm *ovary* in posterior third of body, in front of intestinal junction *uterus* contains large number of terminal-spined eggs	*length* 12-16 mm. *breadth* 0 16 mm. *ovary* in anterior half of body in front of intestinal junction *uterus* contains one, at most three or four lateral-spined eggs	*length* 15-26 mm *breadth* 0 3 mm *ovary* in middle of body *uterus* contains many eggs with abbreviated lateral spine
EGGS			
Size	112-170 x 40-70 μ	114-175 x 45-68 μ	70-100 x 55-65 μ
Shape	oval with conical end	elongated oval	oval to rounded
Spine	terminal	lateral	lateral
Exudate from which recovered	usually urine, occasionally feces	usually feces, occasionally urine	feces only, although eggs are found occasionally in bladder wall
MIRACIDIA			
Gut	small, short	large, extending over nerve mass	small, short
Anterior penetration glands	small, short	large, extending to posterior plane of nerve mass	small, short
Lateral penetration glands	two paired masses with medium separation	two paired masses internally unseparated	two paired masses internally unseparated
CERCARIÆ			
Size			
Body	[illegible]	[illegible]	100-160 x 40-60 μ
Tail trunk	[illegible]	[illegible]	140-160 x 20-35 μ
Furci	[illegible]	[illegible]	50-75 μ long
Anterior sucker	[illegible]	[illegible]	33 μ in transection x 54 μ in length
Penetration glands	2 pairs with large nuclei and finely granular, oxyphilic cytoplasm, 3 pairs with finely granular, basophilic cytoplasm (Best's alum-carmine differentiation)	2 anterior pairs with large nuclei and coarsely granular, oxyphilic cytoplasm; 3 (or 4) pairs with small nuclei and finely granular, basophilic cytoplasm	2 anterior pairs with large nuclei and coarsely granular, oxyphilic cytoplasm, 3 posterior pairs with smaller nuclei and finely granular basophilic cytoplasm
Penetration gland ducts	Moderately thick	Very thick	Very thick
Duct openings	At anterior end of oral sucker, capped by 5 pairs of hollow, piercing spines	At anterior end of oral sucker, capped by 5 (6) pairs of hollow, piercing spines	At anterior end of oral sucker, capped by 5 pairs of hollow, piercing spines
Head gland	Absent	Absent or ephemeral	One large gland present
Germ cells	Several large cells posterior to acetabulum	Many cells at posterior end of body	Clustered mass of cells just behind acetabulum
Second intermediate generation	Sporocyst	Sporocyst	Sporocyst
Known hosts	*Bulinus contortus, B truncatus, B dybowskii, B tropicus, B forskali, B brochii, B innesi, Physopsis africana, P globosa, P. tchadensis, P nasuta, Planorbis dufourii Lymnæa natalensis* (?)	*Planorbis boissyi, P alexandrinus, P pfeifferi, P sudanicus, P. rupellii, Australorbis glabratus A. antiguensis, Tropicorbis centimetralis, Bulinus tropicus, Physopsis africana*	*Oncomelania hupensis, O (Katayama) nosophora O (K) formosana, O quadrasi* (syn *Schistosomophora hydrobiopsis*)

Control.—The problem is particularly important in lake regions which are popular resorts for summer guests, since dermatitis from bathing or swimming produces so much inconvenience that vacations are practically ruined, with considerable loss to hostelries which cater to the summer visitors. Brackett (1939) recommends killing the snails in infested waters by using copper carbonate, particularly along the shallow waters where the snails most frequently breed, in an amount of 3/10,000 pound for each calculated cubic foot of water to be treated. McMullen and Beaver (1945) suggest that protection of beaches of lake from flocks of migratory birds, especially in the fall, may prevent dermatitis the following year.

CHAPTER XIV

TREMATODE PARASITES OF THE INTESTINAL TRACT, BILIARY PASSAGES AND LUNGS

INTRODUCTION

As far as their life cycles are known, all of the species of trematodes which are parasitic in the intestinal tract, biliary passages and lungs of mammals gain access to such hosts as encysted metacercariæ, which are taken in as contaminations of food and drink. The cyst membrane, which has previously been secreted by the cercaria and which enables the larva to pass through the gastric secretions uninjured, is either digested off or weakened by the intestinal juices, so that the activated larva is enabled to break out of its temporary prison and directly attach itself to the intestinal wall or, if a parasite of the biliary passages, after migration, directly or indirectly, into the biliary tracts, to take up its abode in these outpocketings of the intestine. In the case of *Paragonimus*, the lung fluke, the metacercaria, after excystment in the intestinal lumen, penetrates the intestinal wall and migrates to the lungs, where it develops into the adult worm. The trematodes which have been found in the intestinal tract of mammals belong to the suborders **Monostomata**, **Strigeata** (superfamily **Strigeoidea**), **Amphistomata** and **Distomata**. Only members of the groups **Amphistomata** and **Distomata** are known to be parasites of the human intestine. The parasites of the biliary passages of mammals and the lung fluke, *Paragonimus*, all belong to the suborder **Distomata**.

A. AMPHISTOMATE INFECTIONS OF MAN

Suborder Amphistomata (Rudolphi, 1801) Bojanus, 1817.

This suborder is an assemblage of families, all grouped under the superfamily **Paramphistomatoidea**, having the acetabulum caudoterminal, subterminal or ventral, close to the caudal extremity

The amphistomes are at present generally recognized as consisting of six families, **Paramphistomatidæ**, **Gastrodiscidæ**, **Opisthولebetidæ**, **Gyliauchenidæ**, **Cephaloporidæ** and **Microscaphidiidæ**, of which some species are parasitic in lower vertebrates, others in avian hosts, but the vast majority live in the intestinal tract of mammals A very large number of species of amphistomes occur in domestic and wild ruminants, including cattle, sheep and equines. Two species, *Watsonius watsoni* and *Gastrodiscoides hominis*, members respectively of the families Paramphistomatidæ and Gastrodiscidæ, have been reported from man.

Family PARAMPHISTOMATIDÆ (Fischoeder, 1910) emend. Stiles and Goldberger, 1910

This group consists of amphistome species having no ventral pouch

GENUS WATSONIUS STILES AND GOLDBERGER, 1910
(genus named for Dr. Watson of Northern Nigeria)

Watsonius watsoni (Conyngham, 1904) Stiles and Goldberger, 1910 (Watson's fluke).

Synonyms.— *Amphistomum watsoni* Conyngham, 1904; *Cladorchis watsoni* (Conyngham, 1904) Shipley, 1905; *Paramphistomum watsoni* Manson, 1908, *Pseudodiscus watsoni* Fukui, 1929.

Historical Data and Geographical Distribution.—This parasite has been reported only once from man, having been found at the autopsy of an emaciated West African negro who died with symptoms of severe diarrhea soon after admission to a hospital in Northern Nigeria The present author has found it twice in the [illegible] een obtained from the [illegible] Many of the flukes [illegible] numbers were found alive and adherent to the wall of the duodenum and upper part of the jejunum A few were also recovered from the lumen of the large intestine The living worms were described as pear-shaped bodies, reddish-yellow in color, with a translucent gelatinous appearance. They were flattened ventrally and were somewhat indented posteriorly at the margin of the large posterior sucker. The specimens, when preserved, assumed a slaty-brown color.

Structure and Life Cycle.—*Watsonius watsoni* (Fig 61) has a length measurement of 8 to 10 mm., a maximum breadth of 4 to 5 mm. and is 4 mm thick. It is pyriform in shape, being broadest near the junction of the median and posterior thirds of the body The ventral surface is slightly concave, particularly at the margin of the acetabulum; it is surrounded by a convex ridge which becomes inconspicuous anteriorly. The integument is traversed with transverse ridges The acetabulum is subterminal and measures 1 mm. in diameter. The oral opening is ventro-subterminal and is provided with digitate papillæ; the large oral sucker, which lies sunken into the body, is about one-fifth as long as the body and measures 1 2 mm. in transverse diameter. It is provided with a pair of latero-posterior pouches. The esophagus, which arises from the inner median aspect of the oral sucker, first proceeds ventrad, then bends abruptly dorso-caudad. The intestinal ceca spring from its posterior outlet, first arching postero-laterad and then proceeding directly caudad to end blindly just behind the anterior margin of the acetabulum.

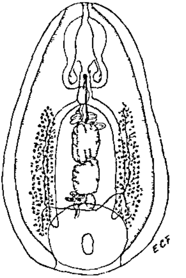


FIG 61 —Adult specimen of *Watsonius watsoni*, ventral view × 6 (After Stiles and Goldberger, Hygienic Laboratory Bull U S Marine Hospital Service)

The excretory system is relatively small and inconspicuous It has been studied only inadequately.

Except for the vitellaria, all of the genital organs lie in the midplane of the body between the intestinal ceca. The testes are squarish in contour, with sharply notched fissures, they lie one in front of the other in the mid-third of the body. The two vasa efferentia, which arise from the anterior aspect of the testes, unite just in front of the anterior testis to form the vas deferens, which proceeds forwards as an intricately coiled tubule In its more posterior portion the vas deferens is thin-walled (vesicula seminalis *s. s.*), but more anteriad it has a muscular wall. At the forking of the gut it suddenly enlarges into a bulbus, the pars prostatica On the anterior margin of the bulbus there arises a thin-walled capillary tubule, the ejaculatory duct which proceeds to the genital papilla The ovary is a rather small,

ovate body, lying behind the posterior testis and slightly to the left of the mid-line. The oviduct, which arises from its dorso-anterior aspect, proceeds dorsad and then caudad to the oötype, which, with its encompassing Mehlis' gland, lies above the ovary. Laurer's canal arises from the dorsal bend of the oviduct and proceeds to the dorsal wall of the worm, where it apparently opens to the exterior. The vitellaria are finely granular aggregations which lie within the anterio-posterior confines of the intestinal ceca but are somewhat extra-cecal in their lateral boundaries. Ducts from these glands join to form a common lateral vitelline duct for each side of the body, the two lateral ducts proceeding mesad in the anterior plane of the acetabulum, uniting just behind the ovary and proceeding as a single, short duct into the mass of the Mehlis' gland, there to join with the oviduct in the formation of the oötype. No seminal receptacle has been described for this worm. The uterus arises from the antero-ventral aspect of the Mehlis' gland and ascends anteriorwards by tortuous coilings, being continued from the level of the esophageal fork as the metraterm and, piercing the muscular region of the copulatory apparatus, opens into the genital papilla just posterior to the ejaculatory duct. The eggs, which vary in size from 122 to 130 by 75 to 80 μ, are described as being similar to those of *Paramphistomum conicum.*

The life cycle of the organism is unknown but, judging from analogy, the cercaria, upon emerging from the molluscan intermediate host, encysts on grass and is thus transferred to herbivores.

Epidemiology.—Man and other susceptible hosts are apparently exposed to infection from ingesting vegetation on which the metacercariæ have encysted.

Pathogenesis, Pathology and Symptomatology.—*Watsonius watsoni* is attached to the mucosa of the duodenum, ileum and cecum, causing inflammation and sloughing of the mucosa, with scar-tissue formation in chronic cases. The infection gives rise to severe diarrhea and toxic inanition, in some hosts probably terminating fatally. Only one case of infection in man is recorded (Africa).

Diagnosis.—Made by finding eggs of the parasite in the stool.

Therapeusis.—Unstudied. *Carbon tetrachloride, tetrachlorethylene* or *crystoids anthelmintic* is probably specific for the infection.

Control.—Unstudied. Since the infection is undoubtedly contracted from ingestion of the encysted metacercaria along with food and drink, thorough heating of such food and water will prevent infection.

Family GASTRODISCIDÆ Stiles and Goldberger, 1910

This group consists of amphistomate species with a discoidal body, divided into a cephalic and a caudal portion.

Genus Gastrodiscoides Leiper, 1913

(*genus from* γαστήρ, belly, and δίσκος, disk, with the suffix εἶδος, like or similar)

Gastrodiscoides hominis (Lewis and McConnell, 1876) Leiper, 1913.

Historical Data and Geographical Distribution.—This amphistome was discovered and first described by Lewis and McConnell in 1876, from material obtained from the cecum of an Indian patient. The worm was redescribed by Stephens from human material *from Assam, and by Leiper, who reexamined the original material* and created the genus *Gastrodiscoides* for it, because of the presence of a genital cone and of the absence of papillæ on the venter The worm has also been found in man

Kamrup district of Assam. In some individuals as many as several hundred worms were evacuated. Khalil has described it from *Tragulus napu* from the Malay States

Structure and Life Cycle.—*Gastrodiscoides hominis* (Fig. 62) is reddish-orange in color when living but becomes creamy-yellow or grayish when preserved. The body is divided into an anterior, conical portion and a posterior, discoidal region. The worm varies in length from 5 to 10 mm. and in cross-section from 4 to 6 mm. In preserved material the anterior cone measures about 2 mm in length and is flattened dorso-ventrally. Its junction with *the disk is gradual and ill-defined. The* prominent genital cone lies slightly behind the mid-plane of the conical portion The acetabulum, which is situated in the caudal portion of the body, is directed ventrad. It measures 2.5 to 4.5 mm in diameter, depending on the amount of its expansion or contraction The integument is aspinose. The mouth is situated anteriad It opens directly into a globular oral sucker. At its slightly constricted posterior margin it gives rise to a pair of lateral pouches and a median prepharyngeal tube The latter leads into a pharyngeal bulb just in front of the origin of the intestinal ceca. The ceca extend pos-ter

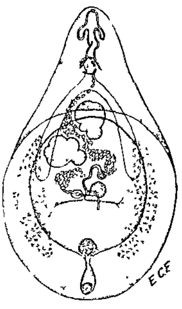


FIG 62 —Adult specimen of *Gastrodiscoides hominis*, ventral view × 10 (Original)

d blindly.
dorsal to the acetabu-
lu

With the exception of the anterior portions of the uterus and of the male duct leading up to the genital cone, the genital organs are all situated in the disk. The testes are large lobate objects, situated somewhat obliquely near the anterior margin of the disk. From the anterior aspect of each testis there arises a vas efferens which unites with its mate to form the vas deferens. The latter becomes dilated along its course cephalad to form the seminal vesicle Both cirrus pouch and pars prostatica appear to be lacking. The male duct opens on the summit of the genital cone just below *the female pore. The rounded* ovary, which is much smaller than the testes, lies in the center of the disk. Just to its right and slightly posterior in position, is Mehlis' gland Connecting these two objects is the oviduct, with an intermediate outpocketing, which has two branches, one

of fan-shaped groups of fine follicular particles near the lateral margins of the disk. Their ducts coalesce to form the lateral vitelline ducts, which are transverse in position and unite on the posterior side of Mehlis' gland and ovary to enter the oviduct just before it proceeds into the oötype. The uterus arises from the right side of Mehlis' gland, coiling first outwards, then upwards, then to the left, from which position it advances in an oblique plane between the testes and then forwards to the genital cone.

Buckley (1939) states that the eggs measure 150 to 170μ in length by 60 to 70 μ in maximum breadth, that they are rhomboidal rather than ovoidal, have a narrow operculum and are pale greenish-brown in contrast to the yellowish-brown eggs of *Fasciolopsis buski*. At a temperature of 80 to 90° F. they become fully embryonated in sixteen to seventeen days. Furthermore, they have a peculiar stickiness. The miracidium, which leaps out of the shell when the operculum pops open, is long and narrow and swims about with a rotary, streamlined movement. It has a prominent apical papilla, a primitive gut about one-third the body-length and a pair of penetration glands, one on each side of the primitive gut, a pair of flame-cells, situated somewhat anterior to the equatorial plane, and is phototactic, although it lacks "eye-spots."

The fate of this worm outside of the mammalian host is unknown. The related amphistomes, *Gastrodiscus ægyptiacus* and *G. secundus*, have been recovered from the horse in Egypt, and *G. minor*, from the pig in Nigeria and Uganda. In Egypt snails of the genus *Cleopatra* are believed to be the intermediate host of *G. ægyptiacus*

Epidemiology.—Unstudied.

Pathogenesis, Pathology and Symptomatology.—*Gastrodiscoides hominis* lives attached to the mucosa of the cecum and the ascending colon, where it causes inflammation of the mucosa with attendant symptoms of diarrhea.

... present in Assam ... stool. ... e evacuation of ... administration of thymol. Buckley (*l. c.*) ... *etrachloride, tetra-* ...

B. DISTOMATE INFECTIONS OF MAN

Suborder Distomata (Zeder, 1800) Leuckart, 1856.

This suborder is an assemblage of families having the acetabulum distinctly precaudal and frequently preëquatorial in position. By far the largest number of trematodes parasitic in man is found in this suborder. All of these species belong to a number of families which, for convenience, have been grouped in the following superfamilies: **Fascioloidea** (Stiles and Goldberger, 1910) Faust, 1929; **Echinostomatoidea** Faust, 1929; **Plagiorchioidea** (Dollfus, 1930) *emend.*; **Opisthorchioidea** (Faust, 1929) Vogel, 1934,

emend, **Troglotrematoidea** Faust, 1929, *emend.*, 1939; and **Hemiuroidea** Faust, 1929, *emend.*, 1939.

Superfamily Fascioloidea (Stiles and Goldberger, 1910) Faust, 1929

Species of this group are now all placed in the type family **Fasciolidæ**. They obtain transfer to their definitive hosts by encysting in or on vegetation or fishes consumed raw by such hosts.

Type Family FASCIOLIDÆ Railliet, 1895 (syn FASCIOLOPSIDÆ Odhner, 1926).

This family consists of only a few known species of large distomes parasitic in land and sea mammals. Two species of the genus *Fasciola* (*F. hepatica* and *F. gigantica*) and the one recognized species of *Fasciolopsis* (*F buski*) have been recorded from man

Genus Fasciola Linnæus, 1758
(genus from *fasciola*, a fillet)

Fasciola hepatica Linnæus, 1758. (The common liver fluke, causing fascioliasis hepatica)

Synonyms — *Distoma hepaticum* Linn., 1758, *Distomum hepaticum* Retzius, 1786; *Planaria latiuscula* Goeze, 1782; *Cladocœlium hepaticum* (Linn, 1758) Stossich, 1892; *Fasciola californica* Sinitsin, 1933; *Fasciola halli* Sinitsin, 1933, etc.

Historical Data and Geographical Distribution.—This fluke, which was the

reported from the North Central States It has been reported from the sheep, ox, goat, camel, llama, elephant, buffalo, dog, horse, ass, several species of rabbits, guinea-pig, squirrel, beaver, deer, roe, antelope, kangaroo, monkey and man It lives in the biliary passages of the mammalian host, where it produces a disease commonly referred to as "liver rot."

Human cases have been reported from Venezuela, Argentina, Puerto Rico, Cuba, Republica Dominicana, Costa Rica, Mexico, Chile, Syria, China, the U S. S R (includi
Hungar
0 6 per

Structure and Life Cycle.—The body of *Fasciola hepatica* is quite large, measuring up to 30 mm. in length by 13 mm. in breadth; it is relatively

the broader, flattened leaf-like body. The posterior end is broadly pointed. The relatively small but conspicuous acetabulum, which is near the base of the cephalic cone, measures about 1.6 mm. in diameter, while the oral sucker averages about 1 mm.

The intestinal tract, which opens inwards from the oral sucker, consists of a well-developed pharynx, a very short esophagus and long intestinal ceca, with secondary and tertiary branches, the ceca extending to the posterior extremity of the worm.

The excretory system, although highly complex, is reducible to a simple fundamental pattern.

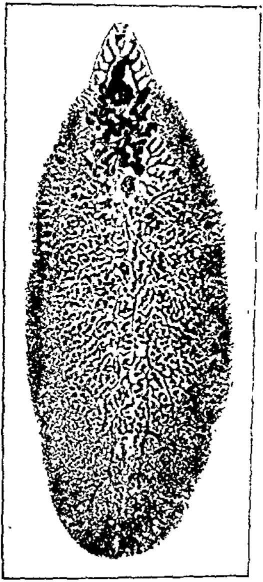


FIG. 63.—Photomicrograph of the adult sheep liver fluke, *Fasciola hepatica* × 4. *ac*, ventral sucker, *gp*, genital pore, *oo*, "oötype," *os*, oral sucker, *ov*, ovary, *t*, *t*, testis, *vil*, vitellaria. (Adapted from Faust, in Brennemann's Practice of Pediatrics, courtesy of W. F. Prior Company, after photograph by Professor H. J. Van Cleave.)

The genital organs are well-developed. The testes are highly dendritic glands, which are situated one behind the other in the second- and third-fourths of the body. From the main anterior stem of each testis there arises a vas efferens, which runs anteriad, paralleling its mate, to the region of the acetabulum, where the two ducts unite at the base of the cirrus pouch. Within the pouch three regions may be distinguished: a posterior

swollen pocket, the vesicula seminalis, filled with spermatozoa; a median capillary tubule, surrounded by prostate glands; and an anterior muscular region, the cirral organ, which opens through the delicate precirral canal into the small genital atrium, and is frequently projected through the genital pore The female organs consist of highly branched vitellaria, which lie in the lateral fields, with a main longitudinal duct for each side which has triangular connections with the transverse ducts, the latter joining one another and entering the "ootype" from the posterior aspect; a highly branched ovary, much smaller than the testes, lying on the right side of the mid-line in front of the anterior testis and opening into the "oötype" through a short oviduct, a short, vestigial Laurer's canal, arising from the left side of the "oötype" and ascending dorsad; the "oötype", a somewhat dilated chamber surrounded by a spherical mass of minute glands (Mehlis' gland), and a uterus, which arises from the right side of the "oötype" anterior to the oviduct and ascends anteriad as a highly coiled, meandering tubule towards the genital atrium. There is no seminal receptacle. The distal extremity of the uterus crosses under the cirrus pouch and opens into the genital atrium at the left of the male organ

Stephenson (1947) found that the adult worms survive *in vitro* for a week, without bacterial disintegration, in a mildly alkaline inorganic medium; that sugars, especially monosaccharides, prolong survival, but that bile salts in the medium are harmful. The optimum pH appears to be about 8.4 *In vivo* the worms feed mainly on blood, converting oxyhemoglobin first to hemoglobin, then to acid hematin. Some hematin is absorbed by the epithelial cells of the gut but the greater portion is concentrated in the worm's feces. The pH of the empty gut is about 6.4

The eggs of *Fasciola hepatica* (Fig. 64) are large operculate objects, having a delicate light-brown color; they measure 130 to 150 μ in length by 63 to 90 μ in breadth. The shells are derived from globules or granules contained in vitelline cells, from orthodihydroxyphenol and a protein. Egg synthesis occurs in the proximal (*i. e.*, inner) segment of the uterus, in the absence of a true oötype The main function of Mehlis' gland is uncertain but it possibly produces a lubricating fluid which stimulates activity of spermatozoa. As the eggs are pushed along through the uterus they become

probably similar to the egg shells of Tubellaria and Cestoidea (Kourí and Nauss, 1938; Stephenson, 1947) Development of the embryo takes place after oviposition. The eggs, which are laid in the biliary tracts, pass into the intestine and are evacuated with the feces.

The development of *Fasciola hepatica*, as first demonstrated by Leuckart and by Thomas, consists in the maturing of the egg (Fig. 65), which requires nine to fifteen days or more at an optimum temperature of 22° to 25° C.; hatching of the miracidium in a favorable aquatic environment, and its active penetration, within a period of eight hours, into the appropriate snail The described molluscan hosts include: *Lymnæa cubensis* (United States, Cuba, Puerto Rico), *L. ferruginea*, *L. modicella*, *L. traski*, *L. buliminoides* var. *techella* and *Pseudosuccinea columella* (United States); *L. attenuata* (Mexico); *L. bogotensis* (Colombia), *L. viator* (Brazil, Uruguay,

Argentina); *L. truncatula* (Faroë Ids., Switzerland, Holland, Jugoslavia, U. S. S. R., North China, South Africa); *L. palustris* (Germany); *L. palustris* var. *sicula* and var. *vulnerata* (Italy, Sardinia); *L. natalensis* (South Africa, Somaliland); *L. brazieri* (Australia); *L. philippinensis* (Phillipines); *L. ollula* (Central China, Japan); *L.* (*Radix*) *auriculata* (North China); *L. plicatula* and *L. pervia* (Shanghai, China); *L. swinhoei* subsp. (Formosa); *L. cailliaudi* (wells of Egyptian oases, in association with *Bulinus truncatus*), and *Bulinus tropicus* (?) (South Africa). Within these and probably other species of *Lymnæa sensu lato* (including subgenera *Lymnæa*, *Galba*, *Radix*, *Pseudosuccinea*, *Succinea*, *Fossaria*, *Praticolella*, *etc.*) metamorphosis into a first generation sporocyst takes place in the lymph channels of that mollusc, and, with the migration of the sporocysts

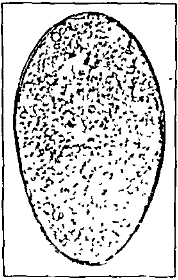


FIG. 64.—Egg of *Fasciola hepatica* Photomicrograph of egg passed in feces of sheep × 450 (Original)

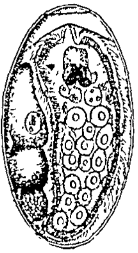


FIG. 65.—Egg of *Fasciola hepatica*, containing fully matured miracidium × 450 (After Thomas, *Quarterly Journal of Microscopical Science*, courtesy of Clarendon Press, Cambridge, England)

into the peri-intestinal lymph spaces, the development of rediæ within the sporocyst. Sinitsin (1933) has described second generation sporocysts *antecedent to the development of rediæ*, as well as rediæ which crawl out of their host. The rediæ, in turn, either produce other rediæ or cercariæ (Fig. 67 *A*), which, on maturing, erupt from the snail tissues in thirty days or more (but only in case water is present, and usually at night), and swim about in the water, at times for as long as eight hours. Sooner or later the cercariæ encyst in the form of little white spherules (Fig. 67 *B*) on various meadow and swamp grasses and water plants, such as cress (*Nasturtium officinale*), or on bark, or free at the bottom of bodies of relatively shallow water. In a moist atmosphere the cyst is quite resistant to usual environmental conditions, but succumbs quickly when dried. Mammals which graze upon, or otherwise consume, such herbage, particularly in a green condition, or [illegible]

The larvæ (n [illegible]

out into the abdominal cavity, thence [illegible] substance of the liver. Eventually they reach the biliary passages, where

they settle down and grow to maturity (Sinitsin, 1915; Suzuki, 1931). Concentrated bile is known to be lethal to the young metacercariæ. It is also possible for the migrating metacercariæ to enter the mesenteric veins or lymphatics, through which they are carried either into the liver, through the liver, or directly into the chambers of the right side of the heart, thence to the lungs and into the general circulation. In the latter instance they may be filtered out in abnormal sites (Bugge, 1928).

The incubation period in the definitive host requires three to four months.

Epidemiology.—The metacercariæ encyst on vegetation growing in swampy meadows or at times the cyst may be deposited in the water near the breeding places of the snails. Circumstantially man is believed to contract the infection by eating raw vegetation on which the metacercariæ

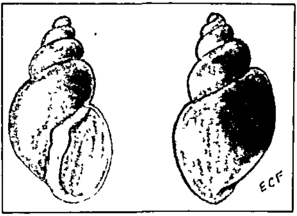


FIG 66—*Lymnæa truncatula*, first intermediate host of *Fasciola hepatica* in the Palæarctic regions × 5 (Original adaptation from Germain and Neveu-Lemaire.)

have encysted. Critical studies on the epidemiology of human exposure to infection have not been consistently carried out, due, no doubt, to the

the cases until

stances human

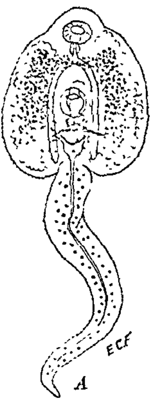
officinale) on

which the metacercariæ have encysted. In Central France the infection in man has assumed epidemic proportions in recent years (Martin *et al*, 1944) Up to 1938 Kourí *et al.* recorded 25 cases from Cuba and Neghme and Ossandon (1943) mention six previously diagnosed infections in addition to their own from Chile.

Pathogenesis, Pathology and Symptomatology.—*Fasciola hepatica*, the liver fluke of the sheep and other herbivorous mammals, causes "liver rot." Cases of sheep liver-fluke infection in man are relatively uncommon, although several hundred genuine cases are on record *En transit* through the liver parenchyma they produce extensive mechanical and toxic irritation, which, in heavy infections, may result in considerable destruction of vital tissues and cause the death of the host. Their presence in the biliary passages causes cystic enlargement of the ducts, adenomata of the biliary epithelium, invasion of leukocytes, including many eosinophils, and the

eventual development of scar-tissue around the ducts. In heavy infections the epithelium is eroded and the young worms may wander back into the liver cells, where abscess pockets are formed. From these pockets the eggs may be extruded into the tissues and set up multiple centers of inflammation. Thus, there is a rapid destruction of the liver parenchyma produced by the migrating young worms, upon which is superimposed the toxic damage, caused by the *mature worms in the biliary passages, resulting in* pressure atrophy of the portal vessels.

Brumpt (1936) recognizes four types of pathological processes produced by the presence of these worms in the biliary passages: (1) Destructive, consisting in the ingestion of blood corpuscles; (2) mechanical, causing obstruction of the biliary passages; (3) irritative, resulting in the hypertrophy of the biliary *epithelium, enlargement of the passages,* and the deposition of sclerified connective tissue in concentric rings around the biliary ducts, with inclusions of eggs and detritus; and (4) toxic and bacteriferous action, due to general absorption into the system of toxic by-products and the invasion of bacteria into ulcerated areas. The ingestion of blood cells is practically negligible. Obstruction of the biliary tracts results in cystic dilatations and, in the *case of heavy infection,* produces profound



A

B

FIG. 67 — *A*, Cercaria of *Fasciola hepatica*, *B*, encysted metacercaria of *F. hepatica* from grass in edemic area × 100 (Original)

icterus. Irritative action gives rise first to hepatomegaly and later to pressure atrophy of the hepatic cells and the portal vessels, resulting in partial or complete cirrhosis of the organ, with accompanying ascites.

Symptoms and signs recorded for human cases include: tender, enlarged liver; hepatic colic, tympanic abdomin eosinophilia up to 70 per cent; irregular fever; more or less persisten *rhea, and, rarely, hemoglobinuria.* Martin *et al.*, (1944) describe a typical case in the following terms: Persistent headache, pain in the right hypochondrium, bilious vomiting; irregular fever, sweating and high eosinophilia

The general toxemia produced by the flukes, especially in heavy infections, results in cachexia aquosa and anemia and is said to be comparable

to "bothriocephalus anemia." Flury and Leeb (1926) demonstrated in experimental dogs that the excreted by-products of these worms are specifically toxic; that the worms possess proteolytic, glycolytic and fat-splitting enzymes; that they can isolate or synthesize egg albumin, and that the degenerating products of dead worms are particularly toxic. In human cases a generalized eosinophilia as high as 54 to 62 per cent may be produced, and the total leukocytes may be temporarily increased to 18,000.

Epidemics of fascioliasis hepatica have been reported from Cuba in 1944 and 1947 (Arenas, Espinosa, Padron and Andreu, 1948). These resulted from eating water cress salad. The primary syndrome, encountered with *great regularity in 52 patients, was referable to hepatobiliary disturbances*, consisting of acute generalized abdominal or epigastric pain, associated with fever between 39° and 41° C., chills and sweating. After persisting for several days there was a gradual or sudden remission of these acute symptoms, succeeded by a sensation of discomfort and fullness in the epigastrium and right hypochondrium, with an associated hepatomegaly. Frequently there was marked systemic intoxication, as evidenced by asthenia, myositis and arthritis, anorexia, urticaria, pruritus and bronchial asthma. The blood picture was unique only in manifesting an average eosinophilia of 35 per cent, although it varied in different patients from 1 to 81 per cent

Ectopic Foci of Infection With Fasciola Hepatica.—In certain instances specimens of *Fasciola hepatica* have been recovered from abnormal situations in the body, such as the bloodvessels, lungs, subcutaneous abscesses, ventricles of the brain and from foci in and around the eye. Diss (1937) collected eight such records from the world literature, while Neghme and Ossandon (1943) added one of their own in which immature *F. hepatica* occurred in a subcutaneous cyst concurrently with mature worms in the proximal biliary passages in association with a syndrome of cholelithiasis. The metacercariæ are even believed to pass from the mother to the fetus. Such findings have led certain helminthologists, among them Braun (1925) and Bugge (1928), to predicate that the worms enter the portal system and from there are distributed throughout the body. This seems to be the most reasonable explanation for the finding of the flukes in these abnormal foci.

In parts of Lebanon and Syria a unique infection of man with *Fasciola hepatica* is said to be quite common. It is locally referred to as "*halzoun*" (*i. e.*, suffocation), and consists in the temporary attachment to the pharyngeal mucosa of adult worms, which have been ingested along with raw livers of goats and sheep, used for sacrificial purposes and later eaten. This localized infection produces an edematous congestion of the soft palate, pharynx, larynx, nasal fossæ and Eustachian tubes, accompanied by dyspnea, [illegible]
Witenbe[illegible]
cases of [illegible]
Moreove[illegible]
upper respiratory congestion in the Near and Middle East. (*Vide* Chapter XXXI.)

False distomiasis hepatica (*i. e.*, due to ingestion of cooked liver of infected

animals containing the adult worms and eggs of *F. hepatica* in the biliary passages) may be mistaken for actual infection. In order to discover if it is real rather than spurious, the patient should be placed under observation for three or more days, during which time liver should be eliminated from his diet. If eggs of *F. hepatica* continues to be passed in his feces, a genuine infection probably exists.

Diagnosis.—This is made from the recovery of eggs of *Fasciola hepatica* (Fig. 63) from the stools, or from bile B and C, obtained through a duodenal sound. Martin *et al.*, (1944) emphasize the importance of early diagnosis. This can be accomplished fifteen days earlier by biliary drainage than by stool examination. Since emetine treatment is more effective against young worms than older ones, the cogency of early diagnosis is readily appreciated. Mazzotti and Osorio (1941) warn against false diagnosis when eggs of *F. hepatica* may be present in raw bile administered perorally and later appear in the feces.

In regions where *Fasciolopsis* is endemic, care must be taken not to confuse the two infections, since the eggs closely resemble each other.

Fasciola hepatica has been demonstrated to stimulate antibody formation in the host, as indicated by precipitin and complement-fixation reactions carried out by several workers. Mazzotti (1942) has reported that *F. hepatica* antigen, prepared by a modified Bachman technic, gives a specific intradermal reaction and is negative for *Onchocerca volvulus* and *Tænia saginata*. Lavier and Stephanopoulo (1944) have also obtained satisfactory diagnosis by immunological and serological methods.

Therapeusis.—Extensive work on the treatment of fascioliasis hepatica in sheep by Railliet, Moussu and Henry, by Marek, and by various British investigators, including Montgomerie, proves the relatively high efficiency of extract of male fern (*filix-mas*), administered in the amount of 0.1 cc. per kilo of body weight and repeated after twenty-four hours. The drug is given either in capsule or in milk. It is lethal to the adult flukes, but will not destroy immature worms present in the smaller bile ducts.

Lièvre (1934) has advocated the use of Magdala rose, using 1 per cent solution, for the eradication of this worm. Mönnig (1934) has found carbon tetrachloride to be highly lethal to the mature worms, although it is recognized as being very toxic. Tetrachlorethylene is not an effective therapeutic. Kourí (1932 *et seq.*) has used emetine hydrochloride with very satisfactory results in treating clinical cases in Cuba. He administers the drug intramuscularly, 3 cgms. daily for seventeen to eighteen days. Rodriguez-Molina and Hoffman (1938) have reported clinical cure and complete disappearance of the eggs of this worm in a patient treated with 4 cgms. of this drug daily for eighteen days. [illegible]

pe [illegible] definitely curative, as demonstrated not only by symptomatic [illegible] also by the permanent disappearance of eggs in the bile and feces. These workers indicate that carbon tetrachloride is effective but dangerous.

In Algeria Fries (1946) has successfully employed carbon tetrachloride combined with emetine hydrochloride in treating a family infected with *F. hepatica*. For the ectopic flukes in various foci in the body no ther-

apeutic procedure other than surgical removal has been developed; for pharyngeal fascioliasis emetics are at times valuable adjuvants.

Prognosis.—Grave in heavy infections. Where only a few worms are present, the amount of liver tissue affected is relatively small, with corresponding *absence of marked symptoms This infection lowers resistance to* secondary bacterial invaders.

Control.—Although the distribution of *Fasciola hepatica* infection in sheep is quite cosmopolitan, human infection is relatively uncommon. Man may also become temporarily parasitized by these flukes from conconsumption of raw infected livers of sheep or goats, which attach themselves to the pharyngeal mucosa and set up severe local inflammation On rare occasions the young worms, excysted in the duodenum, may possibly penetrate through the intestinal wall into the bloodvessels or lymph passages and may be carried to such distant foci as the tissues of the eye (*Distomum oculi humani, Monostomum lentis, Distomum ophthalmobium*), or the brain. Care to eat no raw vegetables or drink no unboiled water in endemic foci is adequate precaution against acquiring the hepatic type of the infection Thorough cooking of infected livers of sheep and goats will prevent pharyngeal fascioliasis.

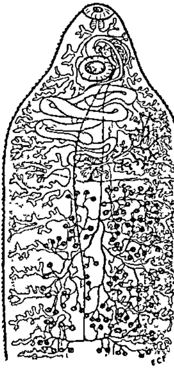


FIG 68 —Anterior end of *Fasciola gigantica*, showing important organs × 6½. (Original)

Eventual extinction of the dangers of infection by this worm may be brought about by its eradication in sheep, cattle and other herbivorous mammals. Such measures as adequate treatment of infected animals, the use of copper sulfate solution (1 to 50,000) or 20 pounds to the acre of swampy pasture land to destroy the snails, and drainage of infected pastures, will help to bring about this desired end. Likewise, *treatment of* sheep with hexachloroëthane-kamala extract will reduce the basic incidence of the disease in reservoir hosts.

Fasciola gigantica Cobbold, 1856. (The giant liver fluke.)

Synonyms.— *Distomum giganteum* Diesing, 1858, *Cladocœlium giganteum* (Cobb., 1856) Stossich, 1892, *Fasciola hepatica* var. *angusta* Railliet, 1892, *Fasciola hepatica* var *ægyptiaca* Looss, 1896

This fluke (Fig 68), which is typically a parasite of the camel (personal communication, Dr Emmett W Price), has been described as a common parasite of cattle and water buffaloes, and to a lesser extent of other herbivores, lives in the biliary tracts of its host The fluke has been found frequently in such hosts in Africa and the Far East Either this species or the closely related *F ægyptiaca* is the common liver fluke of cattle in Hawaii Surveys of these islands show up to 87.5 per cent of

the cattle are parasitized by this worm. There is one genuine record of its occurrence in man (De Govea, 1895), probably contracted in Senegambia (Africa); a second (Codvılle, Grandclaude and Vanlande, 1928), probably contracted in Indo-China, and a third case (Pigoulewsky, 1927), in a seven-year-old child of Tashkend, identified only by eggs in the feces.

The adult fluke is distinguished from *F. hepatica* by its greater length, more attenuate shape, shorter cephalic cone, larger ventral sucker, and by the more anterior position of the testes. The eggs are also larger, measuring 160 to 190 by 70 to 90 μ.

In South Africa the described intermediate hosts are *Lymnæa natalensis* and *Physopsis africana;* in India, *L. (Cerasina) acuminata;* in Hawaii, *L. (Fossaria) ollula*, and in the Philippines, *L. (Fossaria) philippinensis.* In so far as is known the life cycle of this species parallels that of *Fasciola hepatica.*

This worm produces lesions in the liver of its host similar to those of *F. hepatica* infection The patient from Indo-China had a cholecystitis. Diagnosis is based on the recovery of the large operculate eggs from the stool or from biliary drainage. Therapeutic procedure, as tested by Kraneveld on infected cattle and water buffaloes, is similar to that for *F. hepatica.* Prophylactic measures are also identical

Genus Fascioloides Ward, 1917

(genus from *Fasciola*, and εἶδος, kind)

Fascioloides magna (Bassi, 1875) Ward, 1917. (The giant liver fluke.)

This fluke occurs as a parasite in the liver parenchyma and lungs of cattle, deer and other wild herbivorous animals, less frequently of sheep, in North America, but it has not been reported from man.

The life cycle has been worked out by Sinitsin (1930) and by Krull (1933) for the United States and by Swales (1935) in Canada. In the United States *L. (Galba) bulimoides techella, L. (Fossaria) modicella, L. (F.) modicella rustica* and *L. (Pseudosuccinea) columella* have been incriminated, and in Canada *L. (F.) parva* and *L (Succinea) palustris nuttaliana.* The eggs of this fluke are the same size and shape as those of *Fasciola hepatica.* Damage to the liver parenchyma of the infected mammal, particularly sheep, is severe and frequently fatal.

Genus Fasciolopsis Looss, 1899

(genus from *Fasciola*, and ὄψις, resemblance)

Fasciolopsis buski (Lankester, 1857) Odhner, 1902. (The large intestinal fluke, causing fasciolopsiasis.)

Synonyms.—*Distomum crassum* Busk, 1859, *Distomum rathouisi* Poirier, 1887; *Fasciolopsis rathouisi* (Poirier, 1887) Ward, 1903, *Fasciolopsis fulleborni* Rodenwaldt, 1909; *Fasciolopsis goddardi* Ward, 1910; *Fasciolopsis spinifera* Brown, 1917.

Historical Data and Geographical Distribution.—*Fasciolopsis buski* was discovered by Busk in the duodenum of a Lascar sailor who died in London in 1843. The worm was named by Lankaster in 1857 and more fully described by Cobbold in 1859. It is the large intestinal fluke of man and the pig in Central and South China, Formosa, Tonkin, Annam, Thailand, Borneo, Sumatra, Assam, and Bengal, and probably other parts of the Oriental regions. Stoll (1947) has estimated the human incidence of fasciolopsiasis to be ten million, all in eastern Asia. Dogs in Canton are occasionally infected, although they appear to be partially resistant to

infection. Other domestic animals, with the possible exception of rabbits, are apparently refractory to infection. According to Ejsmont (1932), the related species, *Parafasciolopsis fasciolæmorpha*, occurs in the bile ducts of the elk, *Alces alces*, in Poland.

Structure and Life Cycle.—The body of *Fasciolopsis buski* is large; it may be broadly ovate but is more naturally elongated oval (Fig. 69). Fresh specimens have a pinkish, creamy color, and are usually somewhat thicker than fasciolid species, averaging about 2 mm. in thickness. They vary in length from 2 to 7.5 cms., and in width from 8 to 20 mm. They have a spinose integument, but the spines are easily digested off. There is no cephalic cone. The acetabulum, which is directed anteriad, measures up to 2 or even 3 mm. in diameter. The genital pore is immediately preacetabular. The oral sucker, at the anterior end, has an average measurement of 0.5 mm.

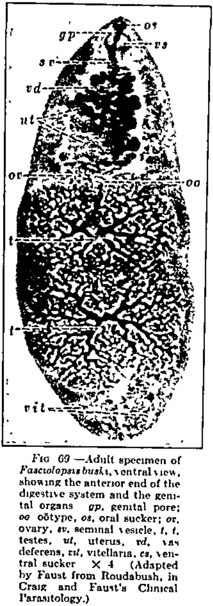


FIG 69 —Adult specimen of *Fasciolopsis buski*, ventral view, showing the anterior end of the digestive system and the genital organs *gp*, genital pore; *oo* oötype, *os*, oral sucker; *ov*, ovary, *sv*, seminal vesicle, *t*, *t*, testes, *ut*, uterus, *vd*, vas deferens, *vit*, vitellaria, *vs*, ventral sucker × 4 (Adapted by Faust from Roudabush, in Craig and Faust's Clinical Parasitology.)

The intestinal tract consists of a very short prepharynx, a bulbous pharynx, and an exceedingly short esophagus which bifurcates in front of the acetabulum to form a pair of unbranched ceca, extending along the medial margin of the vitellaria to the subcaudal end of the worm.

The excretory system of the mature worm is complex and has not been satisfactorily studied.

The highly branched testes (Fig. 69) lie one in front of the other in the posterior half of the worm. From the main trunk of each gland a vas efferens arises, passing forwards with its mate and entering the cirrus pouch at a point half-way between the ootype and acetabulum. According to Goddard, the elongate tubular cirrus pouch contains the following organs: two seminal vesicles, ejaculatory duct, cirral organ, and precirral canal, the latter terminating in the genital atrium. The seminal vesicles are two more or less convoluted tubes, lying side by side within the first portion of the cirrus sac. One of these, the primary vesicle, extends posteriad slightly farther than the other and receives the vasa efferentia. Its distal extremity opens into the secondary vesicle, which narrows to form the ejaculatory duct, which, in turn, continues into

the cirral organ, a muscular tubule lined with delicate spines, as is also the precirral canal. Kobayashi (1930) has described a valve that separates the seminal vesicles from the ejaculatory duct; prostate glands consistently opening into this duct, and a cirrus canal lined with spines, connecting the true cirrus sac with the genital atrium. *This latter is undoubtedly the true* precirral canal.

The oötype lies approximately in the middle of the body. It is surrounded by the ovoid Mehlis' g[illegible]
and surrounded by connective [illegible]
the oötype, consists of three m[illegible]
These open mesad, the lumen [illegible]
passes through Mehlis' gland and proceeds towards the posterior face of the oötype, giving off Laurer's canal in its course, and uniting with the common vitelline duct before entering the oötype. There is no seminal receptacle.

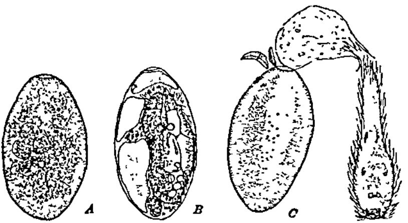


FIG. 70.—Eggs of *Fasciolopsis buski*. *A*, immature egg from feces; *B*, egg with mature miracidium, *C*, miracidium escaping from egg shell. × 200. (After Barlow, Am. Jour. of Hygiene.)

The vitelline follicles occupy the lateral fields of the worm, their main longitudinal ducts each having an anterior and a posterior oblique connection with the transverse vitelline duct of that side. The transverse ducts proceed mesad and fuse to form the common duct on the posterior aspect of Mehlis' gland. The distal end of the tubular ootype gives rise to the proximal end of the uterus, which proceeds through a convoluted course, and is continued at the anterior margin of the acetabulum as the *metraterm*, which opens into the genital atrium.

The eggs are ellipsoidal, rounded at both poles, and are provided with a clear, yellowish-brown, thin shell with a delicate operculum at one end (Fig. 70 *A*). They measure from 130 to 140 μ in length by 80 to 85 μ in breadth. According to Kamisaka (1930), the eggs of *F. buski* may be distinguished from those of *Fasciola hepatica* by the structure of the yolk cells. In the former species the granules of these cells are evenly distributed and the eggs are highly refractive, with clearly visible nuclei. In the latter species the granules are accumulated around the nuclei of the yolk cells and the egg centers appear dark green or dark brown. The eggs are laid continuously into the intestinal lumen and are evacuated with the feces.

The studies of Goddard, Barlow and others in the heavily endemic areas of China and Formosa have conclusively shown that specimens of *Fasciolopsis* from the human host all belong to the same species, while epidemiological and life history data consistently indicate that the porcine species is the same as that found in man.

The life cycle of *Fasciolopsis buski* was first worked out by Nakagawa (1921), utilizing pigs as the definitive host, and later by Barlow (1925) in much more detailed study on the human subject. The cycle closely parallels that of *Fasciola hepatica*. The egg of the worm is immature when voided in the feces of the definitive host (Fig. 70 *A*). The miracidium develops to maturity (Fig. 70 *B*) only after the egg has remained for some time (three to seven weeks) in an aqueous medium at a favorable temperature (80° to 90° F.) After maturity of the larva within the egg shell and ripening of the opercular ring, the larva escapes from its prison (Fig. 70 *C*) and actively swims about for a period of six to fifty-two hours, depending

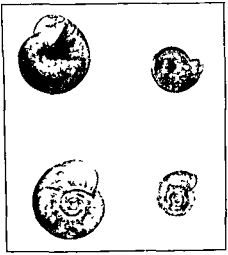


Fig 71 —Molluscan intermediate hosts of *Fasciolopsis buski*. *A*, *Hippeutis schmackeri*, dorsal and ventral views, *B*, *Segmentina nitidella*, dorsal and ventral views. × 2 (Original photographs)

Fig 72 —Sporocyst of *Fasciolopsis buski*, from experimental infection of snail Greatly enlarged (After Barlow, Am Jour of Hygiene)

on the temperature of the water. In the event that there are snails in the immediate vicinity to which the miracidium is adapted, the larva attacks and penetrates any exposed soft part of the mollusc. *Segmentina cænosus*, *S nitidella*, *S. calathus*, *S. hemisphærula* and *Hippeutis schmackeri* are the demonstrated hosts for Central and South China; *S. cænosus*, *S. hemisphærula*, *Gyraulus convex*[illegible] for Formosa; *G. saigonensis* for Tonkin (In[illegible] Assam (India). The molluscan hosts in [illegible] India (except Assam) are unknown. (Fig. 71 *A*, *B*.) On entering the snail and reaching the lymph spaces, the miracidium becomes transformed into a sporocyst (Fig. 72), which is atypical, in that it possesses a functional rhabdocele gut like a redia but lacks a pharynx. From three to four days later rediæ become differentiated within the sporocyst and in nine to ten days emerge free into the lymph spaces. These mother rediæ (Fig. 73) produce only daughter rediæ It is within these latter that cercariæ develop. Upon

maturing (several weeks after the entry of the miracidia into the snail) the cercariæ escape from the daughter rediæ, erupt from the host's tissues and swim vigorously about in the water. However, this period of free-swimming existence is brief, occupying only sufficient time for the cercaria to reach the plant on which the snail is feeding.

The cercaria (Fig. 74) is a heavy-bodied, lophocercous larva, with a length over all of nearly 0.7 mm. It has a well ...
tract ...
in ...

as ... cercariæ find a suitable spot for encystment, they secrete a viscous ... spinose integument. As soon substance from their cystogenous glands. This begins to "set" around the body of each larva within one to three hours. Meanwhile the tail has been

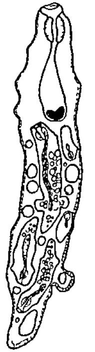


FIG. 73.—Mother redia of *Fasciolopsis buski*, from experimental infection. Greatly enlarged (After Barlow, Am. Jour. of Hygiene.)

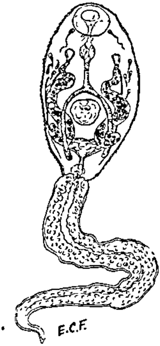


FIG 74.—Cercaria of *Fasciolopsis buski* × 300 (Original)

cast off. The cyst wall consists of an inner resistant layer and an outer friable one. The cysts (Fig. 75) have an average outer measurement of 216 by 187 μ. Various water plants serve as infective agents (vectors) for man and hogs. The most important of these for man are the water caltrop [*Trapa natans* in Chekiang Province, China (Barlow, 1923), *T. bicornis* ...
and ...
T. ...
"chestnut" (*Eliocharis tuberosa*, Fig. 78), although Hung and Doh (1934) and Rose (1936) have also incriminated the roots of the lotus plant and the water bamboo (*Zizania aquatica*) in Chekiang Province, China. Other water plants, including *Vallisneria* sp., *Salvinia natans* and *Lemna polyrhiza*, also appear to be suitable vectors of the cysts. *Eliocharis* is probably the major vector in South China (Fukien and Kwangtung) and Formosa,

and a minor vector in the Yangtze Valley and Grand Canal region of China. The complete life cycle is represented diagrammatically in Figure 79.

The incubation period in man occupies about three months, according to experimental human infection by Barlow.

Fig 75.—Encysted metacercaria of *Fasciolopsis buski.* × 370 (After Barlow Am Jour of Hygiene)

Fig. 76 Fig 77.

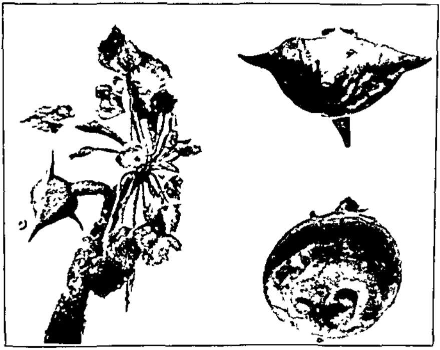


Fig 78.

Figs 76 and 77 —*Trapa natans*, important infective agent of *Fasciolopsis buski* for man in China Fig. 76, plant with attached nut. (After Barlow, Am Jour. of Hygiene); Fig 77, nut obtained from market in endemic region Natural size (Original)

Fig. 78 —*Eliocharis tuberosa*, the common infective agent of *Fasciolopsis buski* for man Natural size (Original)

Epidemiology.—Human infection results most usually from the ingestion of raw pods, roots, stems or bulbs of water plants cultivated in endemic foci where the suitable snails breed. The water caltrop, *Trapa natans* and *T. bicornis*, and the "water chestnut," *Eliocharis tuberosa*, are the vegetable products most commonly involved. The encysted metacercariæ are

attached to the pods of the caltrop and to the "skin" of the "water chestnut." These protective coverings are usually peeled off with the teeth and lips of the consumer. In so doing, the individual sets free some of the cysts, which are then unwittingly swallowed, excyst in the duodenum and develop into adult worms in this region of the bowel. Frequently fasciolopsiasis is familial or institutional in its incidence, or it may involve a high percentage of individuals in a village. Children in particular are subject to infection.

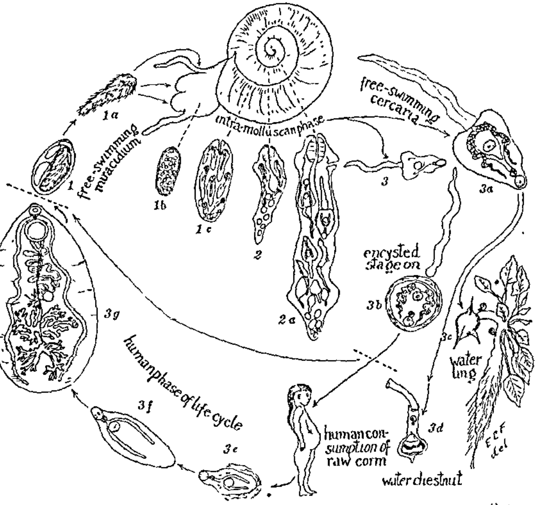


FIG 79 —Diagram ... i. e., egg → miracidium → ... -3g, definitive generation (... dult worm). (Original)

In endemic areas the beds where "water chestnuts" and caltrops are grown are either fertilized with infected human night-soil or are contaminated by promiscuous defecation. Since the suitable snails feed on the plant vectors and man later consumes the infected bulbs, the requirements are met for completing the vicious cycle.

Pathogenesis, Pathology and Symptomatology.—*Fasciolopsis buski* usually lives attached to the mucosa of the small intestine, particularly the duodenum, but it may be found attached to the stomach wall, and at times even

the large bowel. It produces a localized focus of inflammation at the point of attachment. Large numbers of the parasites cause acute intestinal stasis. The lesions occasioned by the presence of the fluke may involve the capillaries of the intestinal wall, producing hemorrhage, or they may provoke abscesses, with infiltration of small round cells and eosinophils. In heavy infections generalized eosinophilia is common.

The first *clinical signs and symptoms* develop about three months after exposure to infection.

In light infections mild symptoms, such as hypogastric pain, may develop. Large r
ing gastric ulcer,
Mangalasmaya (
is usually a diarrhea during the early stage of the infection, which may,

FIG. 80 —Clinical case of fasciolopsiasis buski Face of patient, showing severe edema of cheeks and orbital area (From photograph by Dr C H. Barlow)

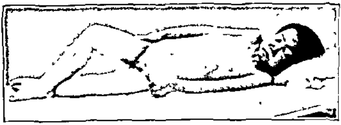


FIG 81 —Body of same child showing edema of abdominal wall and lower extremities (From photograph by Dr C H Barlow)

however, be interrupted by periods of constipation This condition may

extremities (Figs 80 and 81), and at times a moderate ascites According to Barlow, the chest is not involved save in rare fatal cases. Ascites is

common in most instances and in infected children the abdomen is frequently protuberant. On paracentesis many liters of fluid may be withdrawn. During this period generalized abdominal pain is usually noted. The appetite is fairly good, but anorexia, nausea and vomiting may occur and are fairly common accompaniments of heavy infections.

Young (1935) has studied the blood picture in *Fasciolopsis* infection in man, and has found a relatively high leukocytosis in 45.2 per cent of his cases, due primarily to an absolute eosinophilia, which may amount to 33.9 per cent of the total white count. There is usually a neutrophilic leukopenia and, at times, a lymphocytosis. There is no striking alteration of the erythrocyte picture.

In the terminal stage of the infection the skin becomes harsh and dry, diarrhea is continuous and prostration is extreme. Death results from toxemia following anasarca. Human infection is known from Central and South China, French Indo-China, the Malay States, Java, Burma, Assam, Bengal, and possibly other regions of the Orient. Areas of heavy infection exist in Chekiang and Kwangtung Provinces, China.

Diagnosis.—This is based on the finding of *Fasciolopsis buski* eggs (Fig. 70 *A*) in the stool. These must be differentiated from the eggs of *Fasciola hepatica* (Fig. 64), which they closely resemble, from those of *F. gigantica*, which are considerably larger, and from eggs of *Echinostoma ilocanum* (Fig. 83 *A*) and those of other species of echinostomes. The number of worms in a given infection may be estimated by the Stoll technic (see p. 596), since each mature worm lays about 25,000 eggs per day.

Therapeusis.—*Beta-naphthol* (2 administrations of 0.2 Gm. each), which is contraindicated in malaria and in pregnancy, and *carbon tetrachloride* (chemically pure, 3 cc. for an adult, 3 minims for each year of age in children, administered in a single treatment) are specific for the infection. The latter drug is pleasanter to take and is more effective than the former, but must be used with the greatest care, particularly in heavy infections in children. Its use is contraindicated in acute nephritis, marked hepatic dysfunction, pulmonary involvement, pyrexia and in lowered blood serum calcium. The last-named difficulty can be surmounted by feeding calcium lactate (0.5 Gm. or $7\frac{1}{2}$ grains) daily for three or four days before specific therapy is instituted. Pre-treatment and post-treatment purgation with sodium sulfate (Glauber salts) or magnesium sulphate (Epsom salts) is advised. McCoy and Chu (1937), using *crystoids anthelmintic* (caprokol) in amounts of 0.4 gram for children one to seven years of age to 1 gram for children thirteen years and older, produced cures in 54 per

tetrachloride, and is administered in a similar manner, [illegible] equally efficient in evacuating this worm.

Prognosis.—Except in cases of extreme anasarca, prognosis is good, provided the patient is afforded specific treatment. The symptoms soon resolve themselves after evacuation of the worms and the patient proceeds to an uneventful recovery.

Control.—Human infections may be prevented by thoroughly cooking water caltrops and "water chestnuts" in endemic areas, or at least immers-

ing suspected vegetation in boiling water for several seconds The more fundamental problem consists in the sterilization of night-soil in endemic areas.

Superfamily Echinostomatoidea Faust, 1929

This superfamily consists of species which are all placed at present in the

Type Family *ECHINOSTOMATIDÆ Looss, 1902,* emend Poche, 1926

This family, probably not entirely a natural group, comprises an assemblage of many species, of which life history data are known for only a few The cercariæ of some forms encyst within their rediæ, some encyst in the same species or other species of mollusc; others encyst in water after the escape of the cercariæ from the molluscan host; others encyst on vegetation, and still others encyst in the flesh of fishes and frogs The great majority of echinostomes are parasitic in the intestines of lower vertebrates and birds; a few are parasites of the mammalian intestinal tract. Human forms include species of the genera *Echinostoma*, *Himasthla*, *Paryphostomum* and *Echinochasmus*

Genus Echinostoma Rudolphi, 1809, emend Dietz, 1910

(genus from ἐχῖνος, spine, στομα, mouth)

Echinostoma ilocanum (Garrison, 1908) Odhner, 1911. (Garrison's fluke)

Synonyms.—*Fasciolella ilocanum* Garrison, *1908*, *Euparyphium ilocanum* (Garrison, 1908) Tubangui and Pasco, 1933

Historical and Geographical Data—*Echinostoma ilocanum* was discovered and described by Garrison, who found the eggs in the stools of native prisoners in Manila in 1907, and later, after administration of *filix-mas*, obtained twenty-one specimens of the fluke Tubangui (1931) found *Rattus norvegicus* was a natural reservoir of this fluke in the Philippines Human infection is primarily confined to the Ilocano population of Luzon Province, where Tubangui and Pasco (1933) have elucidated the complete life cycle Experimentally the white rat, the cat, and monkeys are suitable definitive hosts Chen (1934) states that this worm was found by him in 13 5 per cent of dogs examined in Canton Bonne, Bras and Lie Kian Joe (1947) have reported this fluke from Java

Structure and Life Cycle—The worm (Fig. 82) is a relatively small, elongated oval object, reddish-gray when alive, measuring 2 5 to 6 5 mm. in length by 1 to 1.35 mm. in breadth and 0.5 to 0.6 mm in thickness, the various measurements largely depending on the contraction or relaxation of the worm At the anterior end there is a circumoral disk, with a breadth of 0 22 to 0.34 mm , separated from the body proper by a slight constriction The disk is surmounted with a crown of 49 to 51 spines, consisting of 5 to 6 spines at each inner ventral angle, lateral to which there are 2 singly disposed spines, then 11 or 12 closely set ones, those of each side being united across the dorsum by an irregularly alternating row of 13 to 15 spines. Posteriorly the worm is attenuated The integument is closely covered with plaque-like scales as far caudad as the posterior testis.

The relatively small oral sucker (0 10 to 0.16 mm in diameter) is situated

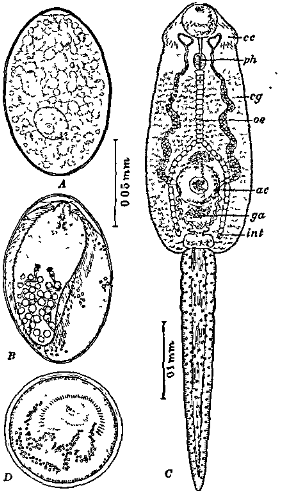
in the center of the oral disk. The acetabulum (0.4 to 0.46 mm. in diameter) lies in the first part of the enlarged body portion. The *pharynx*, which is found almost immediately within the oral sucker, measures 160 μ in length by 110 μ in transverse diameter. It leads into a short esophagus, which bifurcates in front of the acetabulum, the ceca proceeding posteriad to the subcaudal region of the body, where they end blindly. The excretory system has not been studied in the adult worm.

The testes, which lie one behind the other in the middle of the body, are deeply lobed. Vasa efferentia run forwards from the anterior border of each testis to the mid-region of the acetabulum, where they unite into a single deferent duct which enters the cirrus pouch. Posteriorly the pouch contains the vesicula seminalis, which gives rise anteriorly to the long, coiled, cirral organ, the latter frequently protruding through the genital atrium and out of the genital pore. The prostate is lacking. The ovary is situated in the mid-line slightly in front of the anterior testis. It is transversely compressed to globular. Midway between it and the testis is the oötype, with the enveloping Mehlis' gland. The vitellaria are composed of coarse, granular masses, which are extra-cecal in position in the middle third of the body but encroach on the ceca in the posterior third. Practically all of the inter-cecal space between the anterior testis and the acetabulum is occupied with the tightly packed coils of the uterus. The operculate ovoid eggs (Fig. 83, *A*) measure from 83 to 116 μ in length by 58 to 69 μ in breadth. They are immature when passed in the feces, but are fully developed within six to fifteen days after culturing (Fig. 83, *B*).

Fig. 82. Adult specimen of *Echinostoma ilocanum*, ventral view. × 20. (After Odhner, in Zoölogischer Anzeiger, 1911.)

The worms usually live attached by their spine-crowned oral end to the wall of the anterior portion of the small intestine of their host. Development outside of the mammalian body requires two molluscan hosts. The hatched miracidium actively penetrates the first intermediate host through the mantle folds and gill, then migrates to the digestive gland as it metamorphoses into a mother redia. The redia produces daughter rediæ, and they, in turn, produce cercariæ. The complete cycle within this mollusc requires forty-two to fifty days. In the Philippines the following snails have been incriminated: *Gyraulus convexiusculus* (Luzon and Leyte), *Hippeutis umbilicalis* and *Lymnaea swinhœi* var. *quadrasi* (Leyte); in India, *Gyraulus prashadi*, and in the vicinity of Batavia, Java, *G. convexiusculus*. The cercaria which escapes from the snail is typically "echinate" (Fig. 83, *C*). It measures 0.18 to 0.30 mm. in length by 0.10 to 0.13 mm. in maximum width, and has a tail measuring 0.13 to 0.35 mm. long by 35 to 50 μ in diameter. The flame-cell pattern of the cercaria is apparently $2(3 + 3 + 3 + 3 + 3)$.

The cercaria of *E. ilocanum* may encyst in practically any freshwater snail, such as *Bulinus hungerfordianus* (Leyte, P. I.) and *Lymnæa rubiginosa* var. *brevis* (Batavia, Java), but the ampullarids, *Pila conica* (Philippines, Java) and *Viviparus javanicus* (Java) are the most common second intermediate hosts. (See Fig. 83, *D*.) In edemic foci the Ilocanos and natives of Leyte and Mindanao eat *P. conica* without cooking They are prized as food because of their large size, their consumption in the raw state provides opportunity for infection.



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Clinical Data.—The presence of these worms in the digestive tract appears to produce no marked intestinal disturbance. *Filix-mas* is a specific therapeutic.

Echinostoma lindoënse Sandground and Bonne, 1940.

Synonym.—*Echinostoma ilocanum* of Brug and Tesch, 1937.

Morphologically this echinostome closely resembles *E. revolutum*, especially in the possession of 37 collar spines. In the Lake Lindoe district of

Central Celebes the natives are heavily infected with this worm; as many as 249 specimens have been passed following a single administration of tetrachlorethylene. The incidence in some villages ranges from 24 to 96 per cent. The first intermediate host is a small planorbid, *Anisus sarasinorum* or *Gyraulus convexiusculus*, and the encysted metacercariæ are found in pulmonate snails, *Viviparus javanicus* var. *rudipellis et al.*, as well as in the bivalves *Corbicula lindoënsis* and *C. subplanata*. Consumption of the raw molluscs provides the method for man's acquiring the infection. Rats and mice are experimentally good definitive hosts but birds have been found to be refractory to infection.

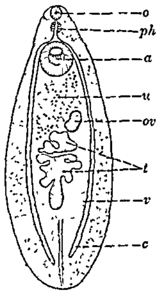

FIG. 84.—Adult specimen of *Echinostoma malayanum*, ventral view × 8. *a*, ventral sucker, *c*, cecum, *o*, oral sucker; *ov*, ovary, *ph*, pharynx, *t*, testes, *u*, uterus; *v*, vitellaria (After Odhner, in Zoologischer Anzeiger 1913.)

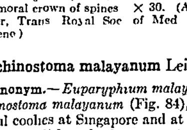

FIG. 85.—Anterior portion of *Echinostoma malayanum*, ventral view, showing circumoral crown of spines × 30. (After Leiper, Trans Royal Soc of Med and Hygiene)

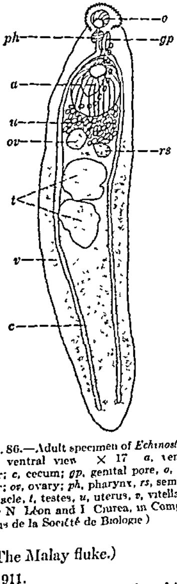

FIG. 86.—Adult specimen of *Echinostoma melis*, ventral view × 17 *a*, ventral sucker; *c*, cecum; *gp*, genital pore, *o*, oral sucker; *ov*, ovary; *ph*, pharynx, *rs*, seminal receptacle, *t*, testes, *u*, uterus, *v*, vitellaria (After N Léon and I Ciurea, in Comptes Rendus de la Société de Biologie)

Echinostoma malayanum Leiper, 1911. (The Malay fluke.)

Synonym.—*Euparyphium malayanum* Leiper, 1911.

Echinostoma malayanum (Fig. 84), which was obtained from the intestine of two Tamil coolies at Singapore and at Kuala Lumpur (F. M. S.), closely resembles *E ilocanum* It has also been reported from man in Java (Bonne, Bras and Lie Kian

Joe, 1947). It differs specifically in being larger (12 mm long, 3 mm. broad and 1.3 mm thick), in having more bluntly rounded ends, in having only 43 circumoral spines (Fig 85), and in having a cirrus pouch which extends to, if not slightly behind, the posterior limit of the acetabulum The vitellaria are also composed of somewhat smaller follicles and are more extensive in their distribution

This species, or a closely related form, is said to be a relatively common parasite

The life cycle of the organism has been partially worked out in India by Rao

Sewell, 1922. The free-swimming cercariæ encyst in the same mollusc and in *Indoplanorbis exustus*, as well as in the barbel, *Barbus stigma*. The molluscan hosts in Singapore and Kuala Lumpur (F M. S) have not been described. Metacercariæ

tetrachloride are all effective in evacuating the worms.

Echinostoma melis (Schrank, 1788) Dietz, 1909. (The Roumanian fluke.)

Synonyms.—*Fascioletta ilocana* Garrison, 1908, of Léon and Ciurea, 1920; *Echinostomum ilocanum* (Garrison, 1908), of Léon and Ciurea, 1920, *Euparyphium jassyense* Léon and Ciurea, 1922

Echinostoma melis was obtained by Léon in 1916 from the diarrheic stools of a patient in Jassy (Roumania) and was first believed to be identical with Garrison's echinostome.

Hsu (1940) reported post-mortem recovery of two worms of this species from the small intestine of a male Chinese who died of chronic myelogenous leukemia. He agrees with Szidat (1940) that his parasites are identical with *E. melis* (Schrank, 1788), which Beaver (1939) found to utilize *Lymnæa (Stagnicola) emarginata angulata* as a first intermediate host and tadpoles as a second intermediate host (region of Douglas Lake, Michigan)

extending from the anterior almost to the posterior extremity The circumoral disk is small, with a width of 0 34 to 0 43 mm It is provided with 27 spines, of which 4 large ones are situated on each side at the ventral angle and the 19 remaining smaller ones are inserted in a double row without dorsal interruption on the border of the disk The acetabulum is large and globose, measures 730 μ in diameter and lies some little distance behind the anterior end The oral sucker is much smaller, averaging about 220 μ in diameter

There is a short prepharynx, a small pharynx, and a capillary esophagus, the gut bifurcating in front of the acetabulum and the ceca extending to the subcaudal region of the worm

The testes, which are situated in the posterior zone of the anterior half of the body, are irregular and somewhat lobate. The cirrus pouch extends somewhat behind the mid-plane of the acetabulum Its posterior portion is filled with the coiled vesicula seminalis and the anterior portion with the cirral organ, the latter being a long muscular cone The genital pore opens slightly in front of the acetabulum. The small spherical ovary lies somewhat to the right of the mid-line, midway be-

tween the anterior testis and the base of the acetabulum. The vitellaria extend from the plane of the ovary to the posterior border of the fluke. In the pretesticular region these follicles are wholly extra-cecal; more posteriorly they encroach on the ceca and in the posterior half of the worm entirely obscure them. The ootype, with

terior testis. In

The uterus fills

The operculate

ovoid eggs measure 132 to 154 μ in length by 79 to 85 μ in transverse diameter.

Nothing is known of the extra-mammalian phase of the life cycle of this fluke in areas where human infection has been reported. The clinical aspects of the infection have apparently not been studied.

Echinostoma revolutum (Fröhlich, 1802). (Frölich's fluke.)

Synonyms.—*Fasciola revoluta* Fröhlich, 1802; *Distoma echinatum* Veder, 1803; *Echinostoma mendax* Dietz, 1909

This echinostome fluke is normally a parasite of species of ducks, geese, fowl, etc , and is cosmopolitan in its distribution. The first human infection recorded was that of a native female Formosan (Anazawa, 1929), recovered after administration of oleoresin of male fern. Bonne, Bras and Lie Kian Joe (1947) report this fluke from Batavia, Java in ducks and chickens, rats, and in two adults and one boy. The

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tively short but it may encroach on the anterior face of the acetabulum. The operculate eggs measure 90 to 126 μ by 59 to 71 μ.

The life cycle of *E. revolutum* involves two molluscan hosts, the first for the development of two generations of rediæ and the cercariæ, the second for encystment of the metacercariæ, although at times encystment may occur within the second generation rediæ. Consumption of the uncooked mollusc infected with the metacercariæ produces infection in the definitive host. Various species of *Lymnæa*, *Physa*, *Paludina*, *Segmentina* and *Planorbis* have been incriminated as first intermediate hosts [1] These same species, as well as *Viviparus viviparus*, *Sphærium corneum* and the limpet, *Corbicula producta*, have been found to be involved as second intermediate hosts.[2] (*Similar index numbers are used in the next paragraph*)

The literature lists the following molluscan hosts with the localities in which they have been found naturally infected *Lymnæa* (*Radix*) *swinhœi* var. *quadrosi*[1] and *L peregrina*,[2] Philippines; *L* (*Radix*) sp.,[1 2] *L* (*Fossaria*) *ollula*[1] and *L. pervia*,[2] Formosa; *L. stagnalis*,[1 2] Italy, *L. swinhœi*,[1] Switzerland; *L. palustris*,[1 2] *L. obrussa*[2] and *L. modicella*,[2] Canada; *L modicella*,[2] Illinois; *L traski*,[2] California, *L attenuata*,[1] Mexico; *Physa gyrina*,[1 2] Canada and Illinois; *P. occidentalis*,[1 2] California; *P attenuata*,[1] Mexico, *P rivaris*,[1 2] Brazil, *Helisoma trivolvis*,[1 2] Canada and Illinois. *H tenuis*,[1] Mexico; *Planorbis cœnosus*,[1] *Segmentina hemisphærula*[1] and *P.* sp,[1] Formosa; *P* sp.,[2] Brazil, *Bulinus pyramidata*[1] and *B pectorosa*,[1] S Australia, *Musculium partumeium*,[2] Maryland; *Sphærium corneum*,[2] *Corbicula producta*[2] and *Viviparus viviparus*,[2] Formosa In addition, experimental infection has been accomplished in *L* (*Pseudosuccinea*) *columella*,[1 2] Maryland and Illinois, *Physa halei*,[2] Maryland, *Pisidium* sp [2] and *Sphærium* sp.,[2] Illinois.

The incidence of human infection with *Echinostoma revolutum* in Formosa has been estimated at 2.8 to 6.5 per cent. Dogs and mice are susceptible laboratory hosts.

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Viviparus chinensis var. *malleatus* is believed to be the second intermediate host *E. recurvatum* (von Linstow, 1873) has been reported as a human parasite in Formosa (syn *E koidzumii* Tsuchimochi, 1924) and in Java (Bonne, Bras and Lie Kian Joe, 1947)

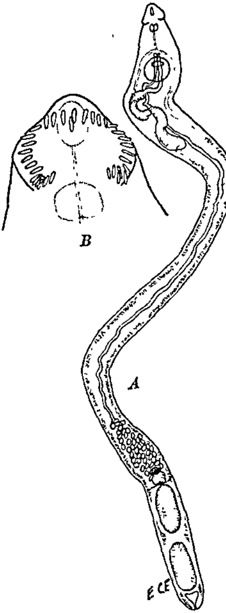

FIG 87 —Adult specimen of *Himasthla muehlensi* *A*, entire worm, ventral view × 15 *B*, anterior end, showing pattern of collar spines (Craig and Faust, adapted from Vogel)

GENUS HIMASTHLA DIETZ, 1909, EMEND. ODHNER, 1910

(genus from ἱμάς, a thong or strap)

Himasthla muehlensi, Vogel, 1933. (Muhlen's fluke)

A single human infection with this previously undescribed echinostome has been reported by Vogel (1933) Five specimens were obtained by Mühlens in Hamburg

after medication with oil of cl
years in Colombia and had tra
the infection from eating seve
route home.

The specimens recovered were already dead, were elongate narrow worms, and measured 11 to 17.7 mm. long by 0.41 to 0.67 mm. broad (Fig. 87). The reniform anterior end measured 337 to 370 μ in breadth and was armed with 32 spines arranged in horse-shoe pattern, without dorsal interruption. Of the total number, two pairs constituted "corner spines." The integument was armed only in the anterior portion. The oral sucker measured 118–145 μ by 94–123 μ, while the ventral sucker, some 880 to 975 μ behind the oral sucker, measured 358–410 μ by 357–425 μ. The elongate oval testes were situated at the posterior end of the body, and Mehlis' gland and minute, transversely oval ovary, just in front of the anterior testis. The cirrus pouch consisted of a very long seminal vesicle, a shorter pars prostatica and a terminal cirrus organ armed with rose thorns. The proximal portion of the uterus was broadly coiled between the vitelline fields, anterior to which it extended as a median, slightly coiled tubule up to the genital pore. The numerous irregularly ovoidal eggs measured 114 to 149 μ by 62 to 85 μ, were indistinctly operculated and immature.

Nothing is known of the life cycle of this species, but by comparison with other species of the genus (Stunkard, 1937), it probably develops through the redia and cercaria stages in a sea-snail or marine bivalve and later encysts in a bivalve. The normal definitive host is probably a sea-gull, the human infection being accidental

Genus Paryphostomum Dietz, 1909, Emend. Bhalerao, 1931

(genus from παρυφή, fringe, and στόμα, mouth)

Paryphostomum sufrartyfex (Lane, 1915) Bhalerao, 1931. (Lane's fluke.)

Synonyms.—*Artyfechinostomum sufrartyfex* Lane, 1915; *Euparyphium malayanum* (Leiper, 1911) of Leiper, 1924 and of Lane, 1924; *Echinostoma sufrartyfex* (Lane, 1915) Faust, 1929.

Historical and Geographical Data.—*Paryphostomum sufrartyfex* was first obtained by a physician on a tea estate in Assam from a girl, aged eight years, suffering from dropsy of the hands and feet and having the general appearance of starvation. One worm was vomited, 5 were passed after administration of santonin, and 57 were passed after administration of *filix-mas*.

The flukes, as received in spirit by Lane, averaged 9 mm. in length, 2.5 mm. broad and 0.8 mm. thick and were curved somewhat ventrad. The description given here is based in part on Lane's study, in part on cotype material from the Indian Museum studied by the present author, and in part from Bhalerao's material from Indian pigs.

Structure and Life Cycle.—The whole of the ventral surface of the worm (Fig. 88) and part of the dorsum are covered with sharp spines deeply embedded in the subintegumentary layer. The spherical acetabulum, which lies well within the center of the anterior third of the body, measures 1 mm. in diameter. There is frequently a more or less pronounced constriction of the body in the region of the acetabulum. At the anterior extremity there is a circumoral disk surmounted by a reniform collar of spines (Fig. 88, *A*), 39 to 42 in number, and all more or less of one size except one pair at the outer ventral angles, which are considerably larger.

In the center of the disk is the oral sucker, measuring 0.13 to 0.2 by 0.15 to 0.37 mm., below which is the pharynx of approximately the same size. The latter leads into a short esophagus, which bifurcates almost immediately, the ceca proceeding first laterad, then caudad, and extending to the posterior extremity where they at times curve inwards.

The deeply lobed testes lie one in front of the other in the posterior half of the body. The vasa efferentia and the vas deferens have not been observed. The cirrus pouch is enormously enlarged, extending from the genital pore in front of the acetabulum more than 0.5 mm. behind the posterior margin of that organ. Within the pouch is an enlarged, uncoiled vesicula seminalis (posteriorly disposed), from the anterior extremity of which there arises the elongate, tightly coiled, tubular cirral organ. Its inner end is surrounded by prostate glands, the outer end is aspinose. The ovary is a small, subglobose body, lying on the right side in front of the

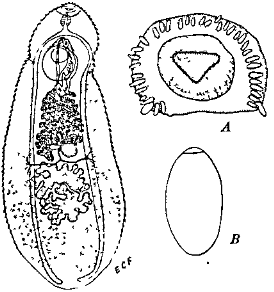

Fig. 88.—Adult specimen of *Paryphostomum sufrartyfex*, dorsal view × 8, (original), *A*, anterior end of body, showing circumoral spines, enlarged, (adapted from Lane), *B*, egg of *P sufrartyfex* × 190 (Original)

encroach on the ceca. On the dorsal aspect they converge posterior to the ovary, while the lateral fields closely approximate one another behind the testes. The transverse vitelline ducts proceed mesad just in front of the anterior testis, and on reaching the mid-plane join each other, to continue anteriad to the oötype, uniting *en route* with the oviduct. The uterus, which occupies the inter-cecal space between the ovary and the acetabulum, consists of coils densely crowded on one another. The metraterm opens through a pore, which with the male pore, is situated in a slight depression

in front of the acetabulum. The eggs (Fig. 88 *B*) are ovoidal and have a well-defined operculum; they measure 90 to 125 μ in length by 60 to 75 μ in transverse diameter, and are immature when laid.

The life history of the worm is unknown.

Clinical Data.—The infection produces a clinical picture similar to *Fasciolopsis* infection, with a profound systemic toxemia. The oleoresin of male fern (*filix-mas*) is specific for removing the worms.

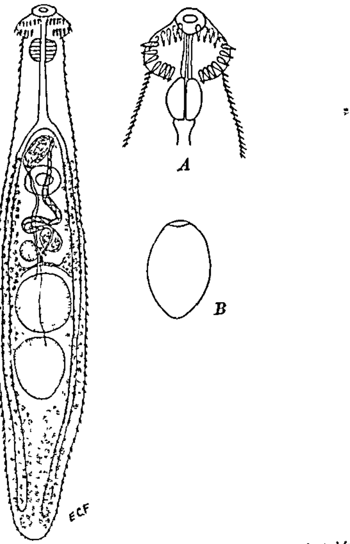

FIG 89.—Adult specimen of *Echinochasmus perfoliatus*, ventral view, × 30, (adapted from von Rátz), *A*, anterior end of *E. perfoliatus*, showing circumoral crown of spines, enlarged (after Tanabe), *B*, egg of *E. perfoliatus*, × 212. (Original)

GENUS ECHINOPARYPHIUM DIETZ, 1910

(genus from ἐχῖνος, spines, and παρυφή, border)

Echinoparyphium paraulum (Dietz, 1909), a natural parasite in the small bowel of ducks, geese, swans, doves, etc., has been recovered once in a human infection in the U. S. S. R. (Skrjabin, 1938).

Genus Echinochasmus Dietz, 1909

(genus from ἐχῖνος, spine, and χάσμα, hiatus)

Echinochasmus perfoliatus (v. Rátz, 1908) Dietz, 1910. (von Rátz's fluke.)

Synonyms.—*Echinostomum perfoliatum* v. Rátz, 1908, *Echinochasmus perfoliatus* var. *shieldsi* Tubangui, 1922; *Echinochasmus perfoliatus* var. *japonicus* Tanabe, 1922.

Historical and Geographical Data.—*Echinochasmus perfoliatus* was first obtained by von Rátz from the small intestine of dogs and cats in Hungary. For some years it has been commonly found as a parasite of dogs and cats in the Far East, as well as from Italy, Roumania and the U. S. S. R. It has also been found in the pig and the fox. In 1922 H. Tanabe reported it as a parasite of man in Japan, and proved that human infection resulted from the consumption of certain fresh-water fishes, uncooked.

Structure and Life Cycle.—*Echinochasmus perfoliatus* (Fig. 89) is an

ventrad. The entire body is covered with spines. The disk-like acetabulum, which is situated at the posterior limit of the anterior third of the body, is appreciably larger than the oral sucker. The anterior end of the worm is surrounded by a circumoral disk which is not continuous across the venter. It is surmounted with a coronet of 24 spines, of approximately equal size. These spines (Fig. 89 *A*) are lacking at the middorsum as well as on the mid-ventral surface

The oral sucker is directed antero-ventrad. It leads into a narrow prepharynx, behind which there is a globose pharynx, followed by a long esophagus. The esophagus bifurcates to form the ceca, which extend to the subcaudal portion of the worm.

The testes are large, globose, or slightly compressed bodies, lying one in front of the other in the mid-longitudinal plane just behind the middle of the body. The vasa efferentia proceed anteriad from the anterior margins of the testes, continuing as delicate tubules over the posterior half of the acetabulum to the cirrus pouch, where they pierce the outer wall of the sac, unite, and become enlarged into the swollen vesicula seminalis. This sperm reservoir completely fills the cirrus pouch, except for a small ejaculatory duct and cirral organ which occupy its anterior portion The male duct empties into a genital atrium immediately behind the bifurcation of the gut.

The ovary is a small globose body, lying on the right side of the mid-line and a little in front of the anterior testis. On the left side, in a slightly more anterior plane, is the receptaculum seminis. The vitellaria extend from the anterior margin of the acetabulum to the posterior end of the body. They occupy

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tubular region surrounded by a few Mehlis' gland cells. The uterus originates from its anterior right aspect and proceeds forwards as a short, only slightly coiled tubule, over the acetabulum to the genital atrium, into which it opens. Only a few eggs (2 to 25) are found in the uterus at any one time. They are ellipsoidal (Fig. 89 *B*), operculate, thin-shelled objects, with a hyaline-greenish hue. They are immature when laid and measure from 90 to 135 μ in length by 55 to 95 μ in transverse diameter.

The extra-mammalian phase of the life cycle is incompletely known. Species of *Parafossarulus* (*P. striatulus* var. *japonicus* et al.) are considered to be the first intermediate host, while various species of fresh-water fishes (including *Pseudogobio esocinus*, *Acheilognathus elongatus* and *A. intermedius*, *Scardinius erythrophthalmus*, *Abramis brama*, *Tinca tinca*, *Esox lucius*, *Aspius aspius*, *Idus idus* and *Blicca björkna*, *Fluvidraco nudiceps*, *Pseudoperilampus typus*, *Gnathopogon elongatus*, *Brevigobio kawabatæ*, *Pseudorasbora parva*, *Zacco platypus* and *Z. temmincki*, *Opsarichthys uncirostris*, *Mogurnda obscura* and *Chænogobius macrognathus*) have been found by experimental feeding to be natural hosts of the infection. Mammals incur the infection through consumption of raw or insufficiently cooked fish. According to Kobayashi (1934) only the gills of these fishes harbor the encysted metacercariæ.

Epidemiology of Echinostomate Infections.—Several of the echinostome infections develop in the definitive host as a result of the consumption of raw fish containing the encysted metacercariæ. In other instances raw snails or other molluscs harbor the metacercariæ. In still others tadpoles and frogs serve as the second intermediate hosts, and thus as transfer agents to the definitive host. Even raw vegetables harbor the cysts of some species of this group.

Pathogenesis, Pathology and Symptomatology of Infections With Species of the Family Echinostomatidæ.—The members of this family which have been recorded from man are apparently only incidental human parasites. They reside in the small intestine, usually near the proximal end, where they are attached to the wall by insertion of their spine-encircled oral ends into the mucosa or submucosa. Judging from infections in reservoir hosts, they appear to produce no more serious damage than flukes residing entirely in the mucosa. Small species, as *Echinochasmus perfoliatus*, are clinically unimportant except in large numbers, when they may provoke an acute enteritis. Medium-sized forms, like *Echinostoma malayanum*, and *E. melis*, provoke a moderate, catarrhal inflammation of the mucosa. Infection with the more fleshy species, *Paryphostomum sufrartyfex*, and probably *Echinostoma ilocanum*, appears to be accompanied by symptoms comparable to those of fasciolopsiasis. Human infection with all of these species is confined to the Orient and to the U. S. S. R., except for the isolated infection with *Himasthla muehlensi*, which was apparently contracted in New York City, and *Echinostoma melis* in Roumania.

Diagnosis.—Made on recovering the eggs from the stool. These eggs are operculate, ellipsoidal objects, varying in color from pale yellow to a yellowish-brown, and in size. (*Vide* description under each species above.) The eggs contain immature larvæ when evaculated in the feces. They require differentiation from those of *Fasciola hepatica*, *Fasciolopsis buski*, *Watsonius watsoni* and *Gastrodiscoides hominis*.

Therapeusis.—Oil of chenopodium and carbon tetrachloride are specific drugs for the elimination of these flukes. The oleoresin of male fern (*filix-mas*) is also effective as a therapeutic agent when *E. ilocanum* and *P. sufrartyfex* are involved. In each case, before administering one of these anthelmintics, specific contraindications should be ruled out, the exact dosage of the drug obtained, and pretreatment and post-treatment purgation with sodium sulfate (Glauber salts) or magnesium sulfate (Epsom salts) carried out.

Prognosis.—Except in heavy infections the echinostomes are usually only minor irritating agents of the mucosa Even in large numbers, save in *P. sufrartyfex* infection, there is no reason for grave concern, although the worms should be eliminated by treatment in order to prevent possible infection from secondary invaders.

Control—*In the case of some of these species, eating of raw fresh-water* fish, tadpoles or frogs, snails or bivalves, should be proscribed; in other cases infection undoubtedly results from eating raw vegetables harboring the encysted larvæ. Salting or inadequate cooking of infected flesh or vegetables will not prevent infection Thorough cooking of all food and boiling all water would exclude all of these infections from the human intestine.

SUPERFAMILY PLAGIORCHIOIDEA (DOLLFUS, 1930) EMEND. MCMULLEN 1937, EMEND NOV. (SYN. DICROCŒLIOIDEA FAUST, 1929 PRO PARTE)

This superfamily consists of a large assemblage of species grouped in the families *Plagiorchiidæ, Dicrocoeliidæ, Lissorchiidæ, Macroderoididæ, Reniferidæ, Haplometridæ, Lecithodendriidæ* and *Microphallidæ*. Human representatives are recorded only from the first two families.

Type Family PLAGIORCHIIDÆ Luhe, 1901

(Syn. Lepodermatidæ Looss, 1901)

The species of this family are small to medium-sized flukes, somewhat elongated, usually slightly flattened; with cirrus pouch and cirrus well developed; ovary pre-testicular, usual on the right; vitellaria well developed, consisting of rather large follicles. Excretory system with a long medium stem and shorter lateral arms. Flame-cell formula: $2[(3 + 3 + 3) + (3 + 3 + 3)]$ Cercaria a polyadenous xiphidiocercaria. Definitive hosts include fishes, amphibia, reptiles, birds and mammals. Species of the genus *Plagiorchis* have occasionally been reported from man

GENUS PLAGIORCHIS LUHE, 1899

(genus from πλάγια, oblique, and ὄρχις, testis)

Plagiorchis philippinensis Sandground, 1940 (syn. *Plagiorchis* sp. of Africa and Garcia, 1937) has been recovered by Africa and Garcia (1935) at an autopsy in Manila, together with specimens of *Echinostoma ilocanum* and *Heterophyes brevicæca*, from the small intestine of a native male Ilocanoan, where the inhabitants eat the grubs of certain insects believed to be the second intermediate hosts of this fluke.

Plagiorchis javensis Sandground, 1940 was obtained as a single specimen at post-mortem of a native Javanese who had harbored a heavy infection of *Echinostoma ilocanum*. The accompanying figure (Fig. 90) illustrates the characteristic features of the species and of the genus.

Plagiorchis muris Tanabe, 1922, a natural parasite of several groups of birds at Douglas Lake, Michigan, employs the snail *Lymnæa* (*Stagnicola*) *emarginata angulata* as second intermediate host. McMullen (1937) obtained experimental infection with this species in mice, rats, pigeons and himself following feedings with the encysted metacercariæ from the snail.

FIG 90.—*Plagiorchis javensis*, adult, from human intestine, Java. × 40 (After Sandground, Rev. Med Trop y Parasitol., Habana.)

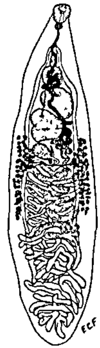


FIG. 91.—Adult specimen of *Dicrocœlium dendriticum*, ventral view. × 10. (Adapted from Braun.)

Family DICROCŒLIIDÆ (Looss, 1907) Odhner, 1910

This family contains a large assemblage of species which are characterized by having the testes in front of the ovary. They live in the biliary (and occasionally in the pancreatic) passages, or intestine, of their vertebrate hosts. The majority of the species are parasites of birds. Two species of the family, which are common parasites of domestic mammals, are recorded from man.

GENUS DICROCŒLIUM DUJARDIN, 1845

(genus from δίχρόος, double, and κοιλία, cavity)

Dicrocœlium dendriticum (Rudolphi, 1818) Looss, 1899. (*The lancet fluke, causing dicrocœliasis.*)

Synonyms.—*Fasciola lanceolata* Rudolphi, 1803 (homonym); *Fasciola dendritica*

coypu and camels. It is frequently associated with *Fasciola hepatica* and occasionally with *Eurytrema*. Genuine human infections are relatively few (Germany, Switzerland, Czechoslovakia, Italy, France, Egypt, Syria, Northern Africa, U. S S R, Java and China)
Soviet investigators (Skrjabin
Berberian (1934), and in Shar
demonstrated the presence of *D dendriticum* eggs in the feces of many persons, few of whom had infections with the worm, many of whom had ingested infected sheep livers and were therefore cases of spurious parasitism

More recently van den Berghe and Denecke (1938) have reported human infection in the Belgian Congo and Roche (1948) in Nigeria

Structure and Life Cycle —The worm (Fig. 91) is lancet-shaped and very flat. It measures from 5 to 15 mm in length by 1.5 to 2.5 mm. in breadth. The posterior end is rounded and the anterior end is attenuate Its integument is aspinose. The acetabulum, which measures about 0.5 to 0.6 mm. in diameter, lies one-fifth the body distance from the anterior end.

The oral sucker is terminal. It leads into a minute globular pharynx and further into a delicate esophagus, which bifurcates some little distance in front of the acetabulum, the ceca proceeding caudad and ending at about the beginning of the terminal fifth of the body.

The excretory system consists of a very long, tubular bladder (Fig 4), with a pore at the posterior end of the body and a pair of lateral connecting tubules, which arise from the antero-lateral aspect of the bladder and proceed latero-anteriad, dividing into anterior and posterior branches in the mid-plane of the ovary. Each branch trifurcates and each fork gives rise to two capillaries, with a flame-cell at the head of each capillary.

The two, slightly lobed testes are situated somewhat obliquely between the ovary and the acetabulum. The vasa efferentia arising from the testes ascend side by side to the anterior margin of the acetabulum, where they join and, entering the bottle-shaped cirrus pouch, enlarge into the coiled

median line and somewhat in front of the equatorial plane The small receptaculum seminis lies behind it and Laurer's canal is situated to the left. These several organs open into the oviduct on its way to the ootype The vitellaria occupy the lateral fields in the middle two-sevenths of the body, encroaching upon the ceca in the region where the transverse ducts arise. These latter are directed mesad and, on uniting in the mid-line, proceed anteriad as a short common duct to join the oviduct before the latter enters the oötype. The ootype is a short, tubular passage surrounded by delicate Mehlis' gland cells The uterus, which arises from the posterior aspect of the ootype, consists of an intricately coiled tube that fills the

inter-cecal field in the posterior three-fifths of the worm, finally ascending on the left side of the median line and proceeding under the left testis and past the acetabulum, to open through the female pore just in front of the male tubule.

The eggs of *Dicrocœlium dendriticum* (Fig. 92) are thick-shelled (with four shell-layers), and are distinctly operculate, with a deep, yellowish-brown color *They measure 38 to 45 μ in length by 22 to 30 μ in breadth,* and are quite resistant to desiccation.

The larvæ are usually mature when the eggs are laid, but they do not hatch wh

hatching

and this mode of entry into the molluscan hosts has been successfully demonstrated by Vogel (1929), Cameron (1931), Skvortsov (1934) and Mattes (1936). The molluscs known to be utilized by this fluke are the following lands snails: *Zebrina detrita, Helicella candidula, H. ericetorum, Euomphalia strigella* and *Abida frumentum* in Germany, *H. ericetorum* and *Cochlicella acuta* in Scotland, *Z. detrita* in Switzerland, *Z. detrita* and *H. ericetorum* in Jugoslavia and *H. unifasciata* in U. S. S. R. (Moscow).

FIG 92 – Photomicrograph of egg of *D. dendriticum* × 450 (Craig and Faust)

Epidemiologic and life history evidence indicates that *Cercaria vitrina* von Linstow, 1887 is the larval stage of the definitive generation. This cercaria (Fig. 93), which is produced following two sporocysts generations within the snail, is an elongated, ovoidal, aspinose larva, varying in body size from 700 μ by 70 μ, when elongated, to 400 μ by 200 μ, when contracted; with a minute stylet directed somewhat dorsad; with subequal suckers; with 12 posterior pairs and 3 anterior pairs of penetration glands, the former being pouch-like and filling a major portion of the body; with an excretory bladder having a long, dilated stem and short, canaliculate cornua, with a flame-cell pattern of: $2[(2 + 2 + 2) + (2 + 2 + 2)]$; *and a long, simple, caudal appendage tapering distally* to a small diameter.

According to Mattes (1936), the cercariæ leave their molluscan host *only when, after a long period of sunshine, rainy weather sets in.* They migrate out of the second generation sporocysts through a cervical birth pore and proceed to the snail's respiratory chamber, where groups of 200 *to 400 secrete slimy, cystogenous material to form a common, spherical* cyst They are passed down to the opening of the respiratory chamber and remain there by their sticky adhesion. Five to fifteen such cystic *masses are expelled and* ...nded

by a thinner slime coati

balls to become attached to plants and other objects.

When *sheep or other herbivorous mammals eat grass containing the* adherent slime balls, they are exposed to infection. The incubation period in sheep has been found experimentally to be three to five and a half *months.*

Epidemiology.—This has not been studied for human infections, because of their relatively rare, sporadic occurrence. However, the mechanism for

infection of sheep and other reservoir hosts consists in the transfer of masses of encysted metacercariæ on grass into the digestive tract of these definitive hosts, the excystation of the metacercariæ and their migration up into the biliary passages.

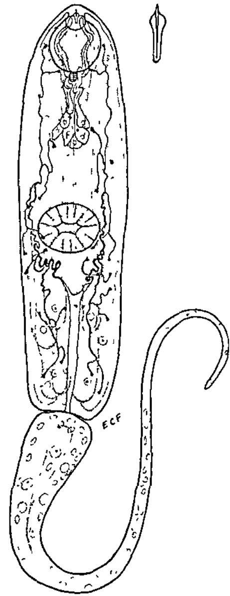


Fig. 93.—Cercaria of *Dicrocœlium dendriticum*, ventral view, showing excretory system and lytic glands. × 188. At upper

Pathogenesis, Pathology and Symptomatology.—In this, as in *Fasciola* infections, the presence of the worms in the biliary tracts gives rise to enlargement of the passages, hypertrophy of the biliary epithelium, scar-tissue formation around the ducts, with gradual pressure atrophy of the liver cells, and eventual portal cirrhosis. Toxemia is much less marked than in sheep liver-fluke infection, probably due to the smaller size of the worms. At times chronic constipation and flatulent dyspepsia, with enlarged liver, and symptoms of toxic depression, have been observed in patients infected with this worm. In other patients diarrhea and vomiting are the cardinal symptoms.

Diagnosis.—Made on the consistent finding of the characteristic dicrocœline eggs (Fig. 92) in the stools, or by duodenal drainage. Care must be used to exclude spurious infections.

Therapeusis.—Galli-Valerio and Bornard (1931) claimed the cure of a patient to whom they administered 0.5 Gm. of thymol three times daily for five days.

Prognosis.—In man the infection is usually not serious and is not known to be fatal.

Control.—Care not to consume grass, cress or other green herbage from endemic meadows and pasture lands, or drink unfiltered water from such endemic areas, constitutes adequate protection for human beings.

Genus Eurytrema Looss, 1907

(genus from εὐρύς, broad, and τρῆμα, "sucker")

Eurytrema pancreaticum (Janson, 1889) Looss, 1907. (The pancreatic fluke.)

Synonyms.—*Distomum pancreaticum* Janson, 1889, *Dicrocœlium pancreaticum* Rail., and Marotel, 1898, *Eurytrema satoi* Kobayashi, 1915.

Eurytrema pancreaticum (Fig. 94), a common parasite of the pancreatic duct of pigs in Hongkong, and also commonly found in the biliary passages of cattle and water buffaloes in the Orient, and occasionally found in the camel (North China) and the monkey (*Macaca syrichta fascicularis*), has been recorded once from man (Hongkong). This fluke differs from *Dicrocœlium dendriticum* in being much stouter and broader, and has slightly ruffled margins. The oral sucker is very large, while the acetabulum is only moderately developed. The deeply notched testes both lie in the posterior plane of the acetabulum, their efferent ducts proceeding mesad and uniting as they enter the cirrus pouch. The cirral organ is long and muscular and is frequently everted far outside the male opening. The ovary is a small, notched organ, situated on the side of the common vitelline duct opposite the oötype. The vitellaria are dendritic follicles lying in the third-fourth of the body, at times encroaching on the ceca. The uterus occupies the entire posterior half of the body between the ceca; it also occupies a considerable area anterior to the right testis The eggs are indistinguishable in size and color from those of *D. dendriticum*.

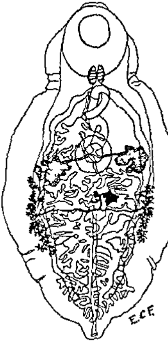


FIG 94.—Adult specimen of *Eurytrema pancreaticum*, ventral view. × 10. (Original)

This fluke produces lesions similar to those of sheep liver fluke infection (*i. e.*, *Fasciola hepatica* infection) In pigs the worm lives in the pancreatic duct and its outpocketings, where it gives rise to a hypertrophy of the epithelium and a walling-off of the duct by scar tissue. The only record from man, cited by Castellani and Chalmers, is from South China

Infections are usually light except in pigs The clinical manifestations are [illegible] pondingly mild

The life cycle of the fluke is unknown, but it seems likely that infection is acquired in a similar manner to that of *Dicrocœlium*. Hence, care not to consume green herbage from suspected meadows presumably affords protection against human infection.

CHAPTER XV

TREMATODE PARASITES OF THE INTESTINAL TRACT, BILIARY PASSAGES AND LUNGS (*Concluded*).

SUPERFAMILY OPISTHORCHIOIDEA (FAUST, 1929) VOGEL, 1934, EMEND. NOV.

THIS superfamily contains several families which may be related phylogenetically or may represent two or more lines of convergent or divergent evolution, depending on whether the cercariæ or the adult stages are taken into consideration as the basis of relationship. Two families, the **Opisthorchiidæ** Braun, 1901 and the **Heterophyidæ** Odhner, 1914, contain species of medical importance.

Type Family OPISTHORCHIIDÆ Luhe, 1901.

These flukes are typically flattened, more or less lanceolate (Subfamily Opisthorchiinæ) or are posteriorly truncated (Subfamily Metorchiinæ); are frequently almost completely transparent in the living state and are provided with weak musculature so that they appear flabby. They lack a genital sucker (*gonotyl*). They commonly inhabit the biliary passages, but at times may be recovered from the pancreatic ducts or duodenum. The metacercariæ are encysted in fishes, less frequently in amphibians The definitive hosts are reptiles, birds and mammals

GENUS OPISTHORCHIS R BLANCHARD, 1895

(genus from ὀπίσθιον, posterior and ὄρχις, testis)

Opisthorchis felineus (Rivolta, 1884) Blanchard, 1895. (The cat liver fluke, causing opisthorchiasis felinea.)

Synonyms.—*Distoma conus* Gurlt, 1831, *nec* Creplin, 1825, *D lanceolatum felis cati* v. Siebold, 1836, *D. felineum* Rivolta, 1884, *D lanceolatum canis familiaris* van Tright, 1889, *D sibiricum* Winogradoff, 1892, *D winogradoffi* Jaksch, 1897, *O tenuicollis* (Rudolphi, 1819), of Ejsmont, 1937

Historical and Geographical Data.—*Opisthorchis felineus* is the lanceolate fluke commonly found in dogs and cats in Central and Eastern Europe. It has been described from man in Prussia, in Poland, and in Siberia, where it is common It is said to be particularly heavy at Kurisches Haff, East Prussia, and in the Ob basin of Siberia. The first human cases were reported by Winogradoff from Tomsk (1892). There are also records of its occurrence in India, Japan and Tonkin (French Indo-China), but it has not been proved to occur endemically in the Sino-Japanese area where *Clonorchis* is prevalent Stoll (1947) has estimated the world incidence of this infection to be 1 1 million, confined almost entirely to Eastern Europe and the U. S. S. R

Structure and Life Cycle.—The adult worm (Fig 95) is a lance-shaped trematode, rounded posteriorly and tapering anteriorly. It measures from 7 to 12 mm. in length by 2 to 3 mm in breadth. Its thickness is only a small fraction of its breadth. On being freshly removed from the biliary tract, the fluke is permeated with a reddish or reddish-orange hue. The

integument is aspinose in adult worms but immature forms may still possess spines. The acetabulum, which measures about 250 μ in diameter, lies about one-fifth the body distance from the anterior end.

The oral sucker, which has the same measurement as the acetabulum, is subterminal and is directed antero-ventrad. It leads directly into a small bulbous pharynx, which is followed by a very short esophagus, the latter bifurcating almost immediately to form the ceca, which extend almost to the posterior end of the worm.

The excretory bladder is a long tubule, occupying the mid-line in the posterior fourth of the body. The pore is terminal. There is an anterior median pocket in front of the openings of the pair of lateral collecting tubules.

The testes are lobed glands, situated obliquely in the posterior fourth of the worm, one to the right and one to the left of the excretory bladder. The two vasa efferentia arise from the anterior aspect of the testes and in the equatorial region of the body unite into a common vas deferens, which ascends anteriad, enlarging *en route* into the slightly coiled vesicula seminalis, which terminates in a weakly muscular ejaculatory duct. The latter proceeds directly to the genital atrium. There is no cirrus pouch. Prostate glands and cirral organ are also lacking. The ovary is a small, ovoidal or slightly lobed body, lying in the mid-plane slightly in front of the anterior pouch

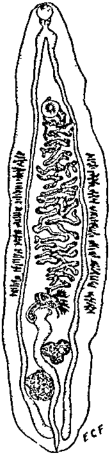


FIG 95—Adult specimen of *Opisthorchis felineus*, dorsal view. × 10 (After Stiles and Hassall, Hygienic Laboratory Bull, U. S Marine Hospital Service.)

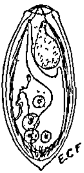


FIG. 96.—Egg of *Opisthorchis felineus* × 1200 (After Faust and Khaw, Am Jour. of Hygiene)

of the excretory bladder. Behind it are the retort-shaped receptaculum seminis (left) and Laurer's canal (right). Immediately to the right is the oötype, with surrounding aciniform Mehlis' gland cells. The vitellaria, which consist of many transversely compressed follicles, occupy the extracecal fields in the middle third of the body. The collecting ducts proceed posteromesad and unite into a short, common vitelline duct, which joins with the oviduct before entering the oötype. The uterus arises from the anterior aspect of the oötype and proceeds anteriad as an intricately coiled

tubule, terminating in the metraterm which opens into the genital atrium beside the male tubule.

The eggs of *Opisthorchis felineus* (Fig. 96) are elongate, ovoidal objects, ... 11 μ.) They possess an ... the shell proper. The ... ts internal organization is asymmetrical.

Hatching of the egg does not occur free in the water, but only after ingestion by certain snails. The known molluscan host in Prussia is *Bulimus leachi* (*Bithynia tentaculata*), in which first generation sporocysts have been found to develop in the vicinity of the rectum. About one month after exposure to infection the second generation (rediæ) leave their mothers (sporocysts) and migrate to the region of the digestive gland. Here the rediæ produce cercariæ, which, while still immature, leave the rediæ (Vogel, 1934). About two months after exposure of the snail to infection, mature cercariæ begin to swarm out. These cercariæ (Fig. 97) are positively phototactic and geotactic and actively seek the ground zone beneath the water. They are pleurolophocercous, have pigmented "eye-spots," possess ten pairs of penetration glands, each with its duct opening dorsal to the oral aperture, and a flame-cell formula of: $2[(5) + (5 + 5 + 5 + 5)]$. The proximal region of the tail is surrounded by an integumentary sheath, which is continued into a nearly transparent dorso-ventral rudder. The body of the living cercaria measures 132 to 172 μ in length by 41 to 48 μ in diameter, and the caudal organ has a length of 400 to 500 μ.

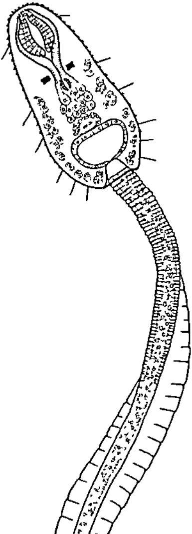


Fig. 97.—Cercaria of *O. felineus*, ventral view. × 330 (Craig and Faust, adapted from Vogel, 1934.)

Vogel (1934) believes that the cercariæ of this fluke attack the fish host only after the fish enters their immediate *milieu*, whereupon they become attached to the scales, drop their tails and penetrate into the tissues. Encystation takes place about twenty-four hours later. According to Ciurea (1917), the following cyprinoid fishes have been found infected: *Idus melanotus*, *Tinca tinca*, *Cyprinus carpio*, *Barbus barbus*, *Abramis brama*, *Blicca*

björkna, *Leuciscus rutilus* and *Scardinius erythophthalmus*. The first two species mentioned are most commonly infected. About six weeks are required for maturity of the encysted metacercariæ within the fish. Excystation occurs almost immediately after the cysts, taken into the digestive tract in raw fish flesh *and digested out of the flesh in the host's stomach*, pass into the duodenum. The freed metacercariæ migrate rapidly up through the ampulla of Vater, then pass into the distal bile ducts, where they become attached to the biliary epithelium and mature in three or four weeks.

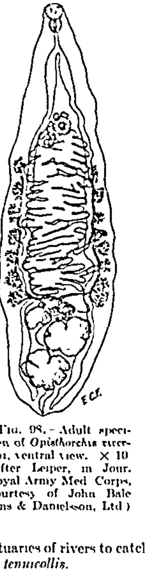


Fig. 98.—Adult specimen of *Opisthorchis viverrini*, ventral view. × 10 (After Leiper, in Jour. Royal Army Med Corps, Courtesy of John Bale Sons & Danielsson, Ltd.)

The entire life cycle of *O. felineus* requires a minimum of four to four and a half months.

Epidemiology.—Human infection, like that of reservoir hosts, results from the consumption of fish flesh, either raw or inadequately cooked, containing the viable cysts of this liver fluke. In *Eastern Prussia and adjacent areas having rivers* flowing into the Baltic Sea, raw fish is a common article of diet, as it is in central Siberia. *Idus melanotus* and *Tinca tinca* are the fishes most commonly infected. These are both important food fishes. It is of interest to note that these fishes are apparently not sources of infection with *Diphyllobothrium latum*.

Opisthorchis viverrini (Poirier, 1886) Stiles and Hassall, 1896.

Opisthorchis viverrini (Fig. 98), which was first described *from the civet cat, F* ... Kerr from autopsies ... ported in about 25 p... country, as determined by stool examination. This species differs from *O. felineus* in the greater proximity of the *ovary to the testes*, the different type and distribution of the vitellaria and the greater tendency of the testes to form deep lobules. The eggs are also shorter and broader (26 by 13 μ), in this respect being more like *Clonorchis* eggs. Infection is undoubtedly acquired through con*sumption of infected raw fish.*

Possibly this species is identical with *O. tenuicollis* (Rudolphi, 1819) Stiles and Hassell, 1896, a parasite of marine mammals (seals and porpoises) which enter the estuaries of rivers to catch fish. If this is the case, then *O. viverrini* is a synonym of *O. tenuicollis*.

Opisthorchis noverca Braun, 1902.

Synonyms.—*Distoma conjunctum* Lewis and Cunningham, 1872, *Amphimerus noverca* Barker, 1911.

Opisthorchis noverca, which was first found in the biliary passages of Indian pariah dogs by Lewis and Cunningham in 1872 and *two years* later by McConnell at the autops... ...the small size of ... nation ... of the ... larger eggs, which measure 34 by 21 μ. The fluke has also been reported ... e wolverene and from the domestic pig (India).

Genus Clonorchis Looss, 1907

(genus from κλών, branched, and ὄρχις, testis)

Morgan (1927) and Price (1940), as well as Dawes (1946) regard the differential characteristics between the genera *Opisthorchis* and *Clonorchis* as insufficient to justify generic separation. Price (*l. c.*) states that *Clonorchis* as a genus "has been retained only because it has become so firmly established in the medical literature"

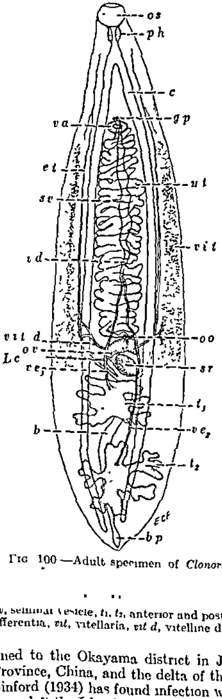
Clonorchis sinensis (Cobbold, 1875) Looss, 1907. (The Chinese liver fluke, causing clonorchiasis.)

Fig 99 —Map showing the distribution of *Clonorchis sinensis* in the endemic areas (After Faust and Khaw, Am Jour of Hygiene)

Synonyms.- *Distoma sinense* Cobbold, 1875, *D spathulatum* Leuckart, 1876, *D hepatis innocuum* Baelz, 1883, *D hepatis endemicum* Baelz, 1883, *D hepatis perniciosum* Baelz, 1883, *D endemicum* Ijima, 1886, *D japonicum* Blanchard, 1886 *Opisthorchis sinensis* Blanchard, 1895, *Clonorchis endemicus* Looss, 1907, *pro parte*.

C. sinensis var. *major* Verdun and Bruyant, 1908, *C, sinensis* var. *minor* Verdun and Bruyant, 1908.

Historical Data.—Cl... McConnell ... described by ... The discovery of the worm in Japan occurred in 1875, although it was not described until 1883, when Baelz recognized both a pathogenic variety (*D. hepatis perniciosum*) and a harmless one (*D. hepatis innocuum*). Various records of the fluke in Chinese patients abroad appeared from 1877 to 1907 but the first information on the infection in the endemic area in China was not published until 1908 (Heanley).



Geographical Distribution.—The distribution of this fluke is confined to the Sino-Japanese areas (Fig. 99), where man, dogs, cats, wild cats, hogs, martens, badgers, minks, and guinea-pigs have been found to be naturally infected. The endemic area extends throughout Japan, Korea, China (except the northwest), Formosa, and French Indo-China, although heavy foci of human infection are confined to the Okayama district in Japan, Southern Korea, parts of Kwangtung Province, China, and the delta of the Red River in Tonkin (French Indo-China). Binford (1934) has found infection with *C. sinensis* in native Hawaiians who have never left the Islands. It is believed that frozen fresh fish or dried or pickeled fish, shipped from Japan or China, are the source of these infections.

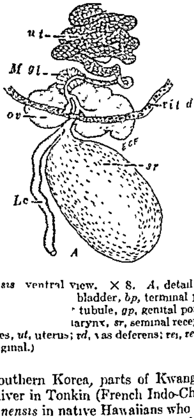


FIG 100.—Adult specimen of *Clonorchis sinensis* ventral view. × 8. *A*, detail of the ... bladder, *bp*, terminal portion ... tubule, *gp*, genital pore; *Lc*, ... larynx, *sr*, seminal receptacle, *sv*, seminal vesicle, *t1*, *t2*, anterior and posterior testes, *ut*, uterus; *vd*, vas deferens; *ve1*, *ve2*, vasa efferentia, *vit*, vitellaria, *vit d*, vitelline duct (Original.)

Stoll's estimated world incidence of clonorchiasis is 19 millions, all in Eastern Asia. While Chinese and to a lesser extent Japanese, Koreans and Indo-Chinese have carried this infection to all parts of the world, there is no evidence that it has ever

become established outside the areas of auchthonous infection in the Far East. Thus, clonorchiasis should not be listed as a quarantinable disease

Structure and Life Cycle.—The adult fluke (Fig. 100) is a spatulate worm, tapering anteriorly and somewhat rounded posteriorly. It is flat, transparent and flabby. The two species (*C. sinensis* and *C. endemicus*), which were created by Looss purely on size differences, are now recognized as a single valid species, with a size range from 10 to 25 mm. in length by 3 to 5 mm. in breadth. The integument of the adult worm is aspinose. The small acetabulum (*va*) is situated at the beginning of the second fourth of the body.

The oral sucker (*os*), which is slightly larger and more muscular than the acetabulum, is directed anteriad. Immediately behind it lies the smaller, globose pharynx (*ph*), posterior to which is the short esophagus. This latter tube bifurcates into two somewhat inflated ceca (*c*), which continue posteriad to the caudal region of the body

The excretory bladder (*b*) is a long, sacculate structure, having a somewhat S-shaped course between the ovary and the posterior end of the body. The lateral collecting tubules (*et*) empty into the reservoir some distance behind the anterior extremity of the bladder. These collecting tubules proceed laterad, then anteriad, to the preacetabular plane, where they appear to divide into much smaller anterior and posterior branches.

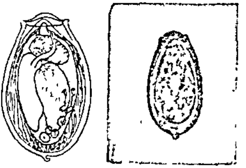


FIG. 101.—Egg of *Clonorchis sinensis*, with enclosed miracidium. Left, × 1200 (From Faust and Khaw, Am Jour of Hygiene), right, × 830 (After Faust, in Brenemann, Practice of Pediatrics, courtesy of W. F. Prior Company.)

The testes (t_1, t_2) are deeply lobed organs lying one in front of the other in the posterior third of the body. From the central mass of each there arises a vas efferens (ve_1, ve_2), which proceeds around the seminal receptacle to a region slightly in front of the ovary, before uniting with its mate to form the vas deferens (*vd*). The latter soon enlarges into the vesicula seminalis (*sv*), which ascends to the genital atrium (*gp*) immediately in front of the acetabulum. The ejaculatory duct is a weakly muscular extension of the seminal vesicle Cirrus pouch, cirral organ and prostate glands are lacking The small, slightly lobed ovary (*ov*) lies in the midplane just under the anterior tip of the excretory bladder. The retort-shaped receptaculum seminis (*sr*) lies to the left at an oblique angle Between it and the ovary is the origin of Laurer's canal (*Lc*), which ascends to the dorsal surface where it opens through a minute pore. The vitellaria (*vit*) consist of minute follicles, occupying the extracecal field in the mid-third of the body. The transverse collecting ducts (*vit d*) proceed mesad, uniting to form a common vitelline duct, which joins the oviduct after the latter has received the common duct from Laurer's canal and the receptaculum seminis, then empties into the ootype (*oo*) Mehlis' gland (*Mgl*), which surrounds the ootype, consists of minute, aciniform cells, forming

a loose tubular investment around the oötype. The uterus (*ut*) arises from the anterior aspect of the oötype, proceeding as a closely coiled and convoluted tubule through the inter-cecal space up to the genital atrium (*gp*), where it terminates.

The eggs of *Clonorchis sinensis* (Fig. 101) vary from 27.3 to 35.1 μ in length by 11.7 to 19.5 μ in breadth, with an average of 29 by 16 μ. They are light yellowish-brown in color, and have the shape of an old-fashioned, carbon-filament electric-light bulb. The operculum fits closely into the shoulder thickening of the shell, like the lid of a sugar bowl. The egg, when laid, usually contains a mature miracidium, which, like that of *Opisthorchis felineus*, is characterized by an asymmetry of internal organs.

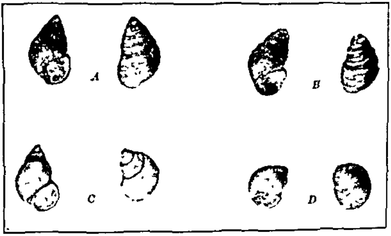


FIG 102 —First intermediate molluscan hosts of *Clonorchis sinensis* *A*, *Parafossarulus striatulus*, *B*, *P sinensis*, probably involved in the Central Yangtze Valley, China, but not yet incriminated, *C*, *Bulimus fuchsianus*; *D*, *Alocinma longicornis*. × 1½ (Original)

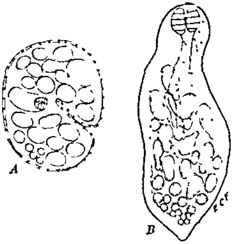


FIG. 103.—First and second intra-molluscan generations of *Clonorchis sinensis* *A*, sporocyst with developing rediæ; *B*, redia (After Faust and Khaw, Am. Jour. of Hygiene)

Hatching of *Clonorchis* eggs does not take place normally outside the body of the appropriate molluscan host. Viable eggs hatch and proceed with their development only after they have been passively ingested by certain species of bithyniid snails. The molluscs which have been reported as incriminated include the following: *Parafossarulus striatulus*, South

China, French Indo-China and Korea; *P. striatulus* var. *japonicus*, Japan, *P. sinensis*, South China, *Bulimus fuchsianus*, South China, *B. chaperi*, Tonkin, French Indo-China; *Alocinma longicornis*, South China; *Semisulcospira honkongensis*, Shaohsing, China; and *Melanoides tuberculatus*, Tonkin, French Indo-China. *Melania* spp. have also been suspected as natural transmitters on Maui Island, Hawaiian Islands, but the infection acquired locally was probably due to infected fish imported from Japan or China. (See Fig. 99.) Hatching of the miracidium may occur in the esophagus, mid-gut or rectum of the mollusc, although it seems most

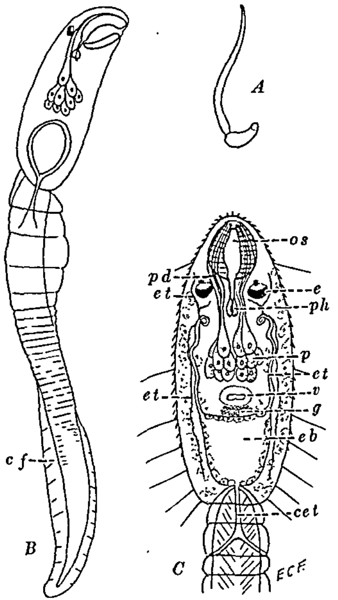


FIG. 104.—Cercaria of *Clonorchis sinensis*. *A*, entire cercaria, × ca. 75; *B*, entire cercaria, × 300; *C*, details of the body and adjacent portion of the tail, × 616. *cet*, caudal excretory tubule; *cf*, caudal fin; *e*, eye-spot; *eb*, excretory bladder; *et*, excretory tubule; *g*, genital primordium; *os*, oral sucker; *p*, penetration glands; *pd*, penetration gland ducts; *ph*, pharynx; *v*, ventral sucker. (Original adaptation from Yamaguti.)

likely that the mid-gut is the usual level of the intestine where this takes place. The miracidium then penetrates through the gut wall into the peri-intestinal lymph spaces, where it metamorphoses into a sporocyst (Fig. 103 *A*), migrates towards the lymph sinuses surrounding the digestive gland and there produces a progeny of rediæ (Fig. 103 *B*). These latter, in turn, produce cercariæ with keeled, lophocercous tails and pigmented "eye-spots" (Fig. 104). The mature cercariæ effect an opening, first in the tissues of the rediæ, then in the taut outer tissue layers of the mollusc, escaping into the water, where they swim about vigorously.

According to Yamaguti (1935), the cercaria (Fig. 104 *A-C*) has a body length of 130 to 170 μ and a body width of 60 to 80 μ, while the tail, with a proximal region surrounded by an integumentary sheath and a distal, dorso-ventral keel (*cf*), measures 330 to 380 μ by 33 to 42 μ. The oral sucker (*os*) is pyriform, measuring 28 to 39 by 22 to 34 μ, and the acetabulum (*v*) is transversely ovoidal. The penetration glands (*p*) consist of four inner and three outer pairs. The genital primordium (*g*) is a compressed mass behind the acetabulum.

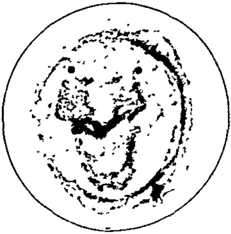


FIG. 105.—Cyst of *Clonorchis sinensis* from fresh-water fish. × 20. (After Faust and Khaw, Am. Jour. of Hygiene.)

On coming within proximity of a fresh-water fish, the cercariæ become attached to the fish, penetrate under the scales and into the flesh, in the meantime discarding their caudal appendages. Forty or more fresh-water fishes of the family Cyprinidæ, less commonly of the families Gobiidæ, Anabantidæ and Salmonidæ in China, Japan, Korea, Indo-China and Formosa have been found infected with *Clonorchis*. The cyprinids constitute the majority of the species and are epidemiologically most important. In South China, where freshly killed raw fish is considered a great delicacy by epicures, the ide, *Ctenopharyngodon idellus*, is the most common source of infection for the human population. Hsü and Khaw (1936) and Hsü and Chow (1937) were able to incriminate only genera and species of the family Cyprinidæ as second intermediate hosts of *Clonorchis* in China. Once within the fish, cystogenous fluid is slowly poured forth through the pores of the metacercaria's integument, "setting" in the form of a spherical or ovoidal wall. The presence of the cyst within the tissues of the fish

provokes a reaction on the part of the host cells, resulting in the deposition of an outer-tissue capsule around the true cyst wall (Fig. 105). Development of the encapsulated larva depends on the amount of nourishment in the immediate vicinity. On consumption of the infected raw fish, the mammalian host becomes infected. In the stomach of the definitive host the cysts are digested out of the flesh and the outer capsule is digested off.

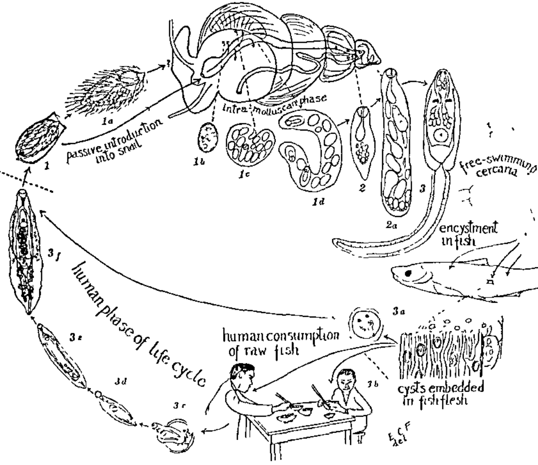


Fig. 106.—Diagram of the life cycle of *Clonorchis sinensis*. *1, 1a–1d*, first generation (i. e., egg→miracidium→sporocyst), *2, 2a*, second, (i. e., redia) generation, *3, 3a–3f*, definitive generation (i. e., cercaria→encysted metacercaria→excysted young worms→adult worms). (Original.)

On passing into the duodenum, the true cyst wall is weakened, so that the activated metacercaria breaks out, secures attachment to the duodenal wall, and migrates to the opening of the common bile duct. It continues its course to the biliary duct and wanders up to the distal biliary capillaries, where it settles down, sheds its integumentary spines and grows to adulthood.

The life cycle of *Clonorchis sinensis* is summarized in the accompanying diagram (Fig. 106).

Epidemiology.—Human infection, like that of reservoir hosts, results from consumption of infected fresh-water fishes containing the encysted metacercariæ. The areas of human endemicity are somewhat more limited

than the areas for reservoir hosts. Thus, in North China autochthonous human cases are relatively uncommon, although there is a heavy incidence in dogs and cats. In the Foochow area of Fukien Province, China rats have been found infected. In the lower classes of the population, particularly the peasants, fish flesh may be eaten raw or it may be inadequately heated by being placed on a steaming pot of rice. On the other hand, the epicures acknowledge their fondness for frankly raw fish flesh, seasoned with condiments. Furthermore, infection may also result from shipment of dried or partially processed fish from the endemic areas to distant countries.

Genus Pseudamphistomum Luehe, 1908

(genus from ψευδής, false, ἀμφί, double, and στόμα, mouth)

Pseudamphistomum truncatum (Rudolphi, 1819) Luehe, 1908.

This fluke, which may possibly be a parasite of man in Siberia, has been reported from the biliary passages of the seal, cat, dog, fox and wolverene (*Gulo borealis*). It is recognized by the squarish pseudo-sucker-like posterior end of its body and, like other adult members of the subfamily **Metorchiinæ**, by the possession of a spinose integument. The egg, measuring 29 by 11 μ, can hardly be differentiated from that of *Opisthorchis felineus*.

While the life history of this species is unknown, H. Tanabe (1921) has found that infection with another species (*Metorchis orientalis*) of the same subfamily is contracted from eating the fish *Pseudorasbora parva*.

Pathogenesis, Pathology and Symptomatology of Infections with Species of the Family Opisthorchiidæ.—*Opisthorchis felineus*, *O. viverrini*, *O. noverca* and *Clonorchis sinensis*, which are all similar, in possessing flattened, transparent, ellipsoidal bodies with very poorly developed musculature, live typically in the distal capillaries of the biliary passages. They are more commonly present in the left liver lobe than in the right lobe, due to the fact that the path of migration into the former region is more direct than into the latter. Here these flukes may live for a period of five to twenty or more years. Except in very heavy infections the main portion of the liver tissue is relatively little modified. The changes induced by the parasites are essentially those recognized by Brumpt (1936) for *Fasciola hepatica* namely, (1) destructive action, (2) mechanical effect, (3) irritative action and (4) toxemia.

The *destructive action* consists in desquamation of the biliary epithelium and the ingestion by the fluke of blood cells. Such cases are common but appear to have only slight effect on the general condition of the host. The blocking of biliary passages (*mechanical effect*), resulting in biliary stasis, is relatively uncommon and seldom results in generalized icterus. In a series of several hundred animals experimentally infected with *Clonorchis sinensis* by the present author only three (two cats and one guinea-pig) showed evidences of jaundice. The *irritative action* produced by these flukes consists of marked proliferation of the biliary epithelium, with crypt formation and multiple production of new biliary capillaries; periportal connective tissue hyperplasia; and fibrous tissue formation around "graves of eggs." There is, however, no true giant-cell tubercle around these eggs,

as there is in schistosomiasis. There appears to be *no marked generalized toxemia* as in sheep liver fluke infection. Nevertheless, the changes in the walls of the biliary ducts occur in areas which worms are too large to reach, so that the determining factor in such instances may be the toxic secretions of the flukes. While *bacterial invasion* may play a secondary rôle in ulcerative processes developed in opisthorchid- or clonorchid-infections, the classical picture has been shown to be produced by these flukes in bacteria-free biliary passages. In heavy infections the pancreatic duct, as well as the biliary tract, is at times involved.

The lesions in animals infected with *Clonorchis*, species of *Opisthorchis*, etc. are referable to three progressive stages. The lesions of the first degree consist primarily of proliferation of the biliary-tract epithelium, extensive infiltration of wandering cells and leukocytes around the portal spaces and interlobularly along the vessels, and the gradual thickening of the walls of the biliary passages through connective-tissue proliferation (Fig. 107 *A*) In those of the second degree the walls become greatly thickened and the liver parenchyma of adjacent zones is involved, due to the pressure of the growing connective tissue (Fig. 107 *B*). In the lesions of the third-degree, cirrhosis of the liver cells and destruction of the parenchyma are quite complete (Fig. 107 *C*)

Cases of human infection with only a few worms probably never go beyond the first stage. In moderately infected persons (several dozen to hundreds of worms) the second type may be attained. In a study of 66 postmortem cases in China, Hoeppli (1933) found evidence of considerable histopathology. Only in endemic areas of severe infection, where there is opportunity for continuous reinfection, is the advanced stage likely to be attained. Regions where such a degree of infection for clonorchiasis occurs are the Okayama district in Japan, certain local areas in Kwangtung Province, China, and the Tonkin delta, French Indo-China. For infection with *Opisthorchis felineus* such districts are found in East Prussia and in the vicinity of Tomsk, Siberia. The data on the incidence of *O. viverrini* and of *O. noverca* are too inadequate to determine the severity of infection.

Inouye (1903), who studied the symptomatology of *Clonorchis* cases in the Okayama endemic area, Japan, recognized (1) a mild type, without appreciable symptoms (correlated with the first-degree changes of the liver); (2) a secondary stage, attended by diarrhea, edema, and hypertrophy of the liver (corresponding to second-degree lesions of the liver); and (3) a severe type, with symptoms of the secondary stage, but aggravated by involvement of the hepatic portal circulation (due to hepatic cirrhosis). The common symptoms consist of irregularity of appetite, with a feeling of fullness and pressure after meals, and diarrhea. There is no significant modification of the blood picture, except at times there may be an appreciable eosinophilia (5 to 47 per cent recorded in uncomplicated cases). In light infections Chen and Faust (1949) have at times found a moderate loss in weight and some impairment in liver function as indicated by the cephalin flocculation test. Experimentally there is evidence of hyperplasia of the bone-marrow, both with respect to the eosinophils and the reticulo-endothelial system. Mild cases usually go unnoticed unless diagnosed by the finding of the eggs in the stool. The more advanced

...of the first degree, confined to
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cases must be differentiated from malignancies of the liver, hydatid cyst, beriberi, and from the usual types of hepatic cirrhosis.

Otto (1935) is convinced that the occlusion of the larger bile ducts by masses of eggs and by tissue proliferation constitutes a serious pathological entity, producing a chronic catarrhal cholangiitis, which becomes more pronounced as the bile becomes more viscid. He also suggests that the detoxifying properties of the liver may be seriously impaired, and systemic toxemia may result, as indicated by cardiovascular symptoms, including palpitation of the heart and tachycardia, vertigo, tremors, tetanic cramps and mental depression.

Diagnosis.—This is based on the finding of eggs (Figs. 96, 101) of these flukes in the stool. Probably the most efficient method for concentration of these eggs is the $HCl\text{-}Na_2SO_4$-Triton-Ether technic, recommended by Faust, Ingalls and See (1946) for recovery of *Schistosoma japonicum* eggs from the stool and tested for eggs of *Clonorchis sinensis* by Chen and Faust (1949). (See Section VII, under "Concentration Methods—Acid-Ether Technics." At times it may be desirable to obtain eggs for determinative diagnosis by biliary drainage. The eggs require to be differentiated from those of heterophyid flukes.

Therapeusis.—Sodium antimony tartrate, administered intravenously, is helpful in reducing the number of worms in the biliary passages (Shattuck, 1924). Kagy and Beaver (unpublished study) were not able to produce complete eradication of *Clonorchis* in a light chronic clinical infection by use of potassium antimony tartrate, although they temporarily reduced the egg output to zero. Erhardt (1932) obtained excellent results in *Opisthorchis felineus* infection in cats by administering fuadin (neoantimosan) intramuscularly (0.4 cc. per kilogram of body weight) Chen and Faust (1949) employed fuadin on two mild clinical infections and provided evidence of a sustained reduction in egg output to a small fraction of the pre-treatment number. Clinical improvement was noted, with gain in weight and reduced cephalin flocculation reaction. After a third course of treatment with this drug the stools became free of eggs and remained so during follow-examinations for a period of months, but later were found to have a reactivated egg production. The penta- and hexa-methyl rosanilins (gentian violet, crystal violet and methyl violet), administered orall [illegible]
per [illegible]
intra [illegible]
nate or every third day, until a total of not more than 6 grams of the dye has been given, will kill all of the worms which can be reached by the dye in helminthicidal amounts In early cases this may result in complete cure, in chronic cases the number of worms may be reduced from one-half to nine-tenths (Faust and Yao, 1926; Kawai, 1937) Otto and Tschan Tsching (1935) have reported moderately successful results in treating clonorchiasis with gold salts by the intravenous route. The amount of reduction in egg-production as an index of the number of worms present, may be determined by the $HCl\text{-}Na_2SO_4$-Triton-Ether Concentration, Technic. See Section VII, "Concentration Methods—Acid Ether Technics.")

Prognosis.—In light infections clinical symptoms are frequently negligible. In heavier infections there is probably considerable loss of vitality and

possibly a lowering of the bodily resistance to other diseases, but such cases almost never die of fluke infection. Heavily *infected patients* develop irreparable loss of active liver tissues and in such cases death is ultimately due to the parasites.

Control.—These infections may be prevented by the thorough cooking of *all fresh-water fish* intended for consumption. In South China and French Indo-China, where fishes are killed in the presence of the feaster and the flesh is then eaten raw after seasoning with condiments, educational efforts *should* be effective in reducing exposure to infection. In endemic areas the addition of ammonium sulfate to fresh night-soil is *recommended* as a sterilizing agent.

Family HETEROPHYIDÆ Odhner, 1914

This *family* consists of very small trematodes, oval, pyriform or elongate-oval in contour, with the integument thickly beset with minute scale-like spines. The worms have well-developed oral and ventral suckers, while the genital pore, which is situated near the ventral sucker, is typically provided with a genital sucker (the *gonotyl*), which may be fused with the *ventral sucker. The adult worms all live in the small intestine* of their host, which is a fish-eating bird or mammal. The small, operculate eggs contain bilaterally symmetrical miracidia, which are fully mature when laid. Species of Melaniidæ and Bithyniidæ, and possibly other molluscs, are utilized as first intermediate hosts, and fresh-water fishes as second intermediate hosts. The cercariæ are pleurolophocercous, "eye-spotted" organisms, which are distinguished with difficulty from those of the **Opisthorchiidæ**. Infection of the definitive host results from consumption of infected raw fish.

The flame-cell formulæ of members of the family **Heterophyidæ** are not consistent with one another: *Heterophyes*, $2[(3+3)+(3+3)]$; *Centrocestus* and *Cæcincola*, $2[(2+2)+(2+2)]$; *Cryptocotyle*, $2[(3+7+7)+(7+7+7)]$; *Rossicotrema*, $2[(2+3)+(3+2+3)]$. An adequate *explanation for this exception* to the general rule has not been offered. However, Hopkins (1941) states that "if genera which had been placed in the same family were found to have widely different flame cell formulæ, it would certainly cast doubt on the closeness of their relationship, especially if the difference were found in the cercariæ as well as in the adult stages."

GENUS HETEROPHYES COBBOLD, 1866

(genus from ἕτερος, different, and φυή, shape)

Heterophyes heterophyes (v. Siebold, 1852) Stiles and Hassall, *1900*. (von Siebold's fluke.)

Synonyms.—*Distoma heterophyes* v. Siebold, 1852; *D. heterophyes hominis*

Railliet, 1890; *Cœnogonimus heterophyes* Looss, 1899;

Luhe, 1899; *Heterophyes nocens* Onji and Nishio, 1915.

Historical and Geographical Data.—This minute, pyriform fluke has been found in natural infections of the cat, dog, fox and man. Its known dis-

tribution includes Egypt and the subtropical moist belt of the Far East (*i. e.*, Japan, Southern Korea, Central and South China and Formosa) The worm was discovered by Bilharz from an autopsy in Cairo in 1851 and is now known to be a common parasite of man in the Nile delta, where hundreds of the flukes may be attached to the intestinal mucosa of the human host

Structure and Life Cycle.—*Heterophyes heterophyes* (Fig. 108) is an elongated, pyriform worm, with a broadly rounded posterior and a more pointed anterior end. It measures 1 to 1.7 mm. in length by 0 3 to 0 4 mm in breadth The integumentary scales which cover the body are relatively narrow and close to one another; they are more numerous at the anterior end than towards the posterior part of the body. The acetabulum is a very muscular, thick-walled organ, situated at the beginning of the equatorial third of the body. It measures 230 μ in diameter. The genital sucker, which lies adjacent to the left posterior aspect of the acetabulum, has an average diameter of 150 μ. Some 60 to 90 chitinous rodlets are set into the genital sucker (Fig. 108).

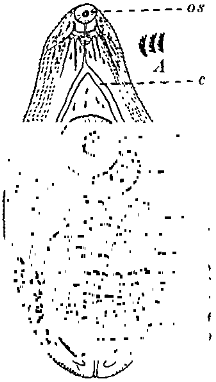

FIG 108 —Adult specimen of *Heterophyes heterophyes*, ventral view × 50 *c*, cecum, *ex b*, excretory bladder, *g*, gonotyl, *oo*, oötype; *os*, oral sucker, *ov*, ovary, *sr*, seminal receptacle, *sv*, seminal vesicle, *t*, testis, *ut*, uterus, *vit*, vitellaria, *vs*, ventral sucker (Adapted from Looss) *a*, detail of spines of genital sucker

The oral sucker is much smaller, averaging about 90 μ in diameter. It leads into a capillary prepharynx, followed by a minute bulbous pharynx, then a capillary esophagus, which soon bifurcates to form the intestinal ceca, the latter gradually separating from one another until they reach the lateral aspects of the worm, then proceeding posteriad and finally terminating at the rounded posterior part of the body.

The excretory bladder is an elongate tube which reaches to the region of the receptaculum seminis, where it receives the lateral collecting tubules. The flame-cell formula is: $2[(3 + 3) + (3 + 3)]$.

The two ovoidal testes are situated slightly obliquely, just in front of the posterior bend of the intestinal ceca. The vasa efferentia are given off from the anterior end of the testes, proceeding forwards and mesad and uniting in front of the ovary to form the vas deferens This common tubule soon enlarges into the coiled, retort-shaped vesicula seminalis, which first bends to the right and then leads into the muscular ejaculatory duct, which ascends to the genital atrium within the sucker. It is surrounded near its outer end by prostate glands. Cirrus sac and cirral organ are lacking.

The ovary is a subglobose organ, lying in the mid-line near the anterior margin of the posterior third of the body. Its short duct leads posteriad, where it is joined by the receptaculum seminis from the lower right aspect and by Laurer's canal from the lower left. These all lead out through a common duct, first anteriad, then, after receiving the common vitelline duct, proceeding dextrad over the ovary to the oötype. There are about fourteen large, polygonal, vitelline follicles on either side of the body, of which seven are extra-cecal in positon. The oötype, which lies in a transverse position, is surrounded by a minute Mehlis' gland. The uterus arises from its right aspect, coiling intricately through the interceeal field of the worm, and finally ascending to the metraterm beside the male opening within the genital pore.

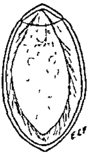

FIG 109.—Egg of *Heterophyes heterophyes*. Camera lucida drawing of egg from feces kindly sent the author by Dr. C H. Barlow, Cairo, Egypt × 1120. (Original)

The eggs (Fig. 109) of *Heterophyes heterophyes* are operculate, ovoidal objects, with a slight suggestion of a shoulder thickening at the insertion of the opercular cap. They are light brown in color and measure 28 to 30 by 15 to 17 μ.

The life cycle of *Heterophyes heterophyes* has been elucidated by Khalil (1923, 1933) in Egypt. Invasion of the snail (*Pironella conica*) is passive; the intramolluscan generations consist of a mother sporocyst and a redia

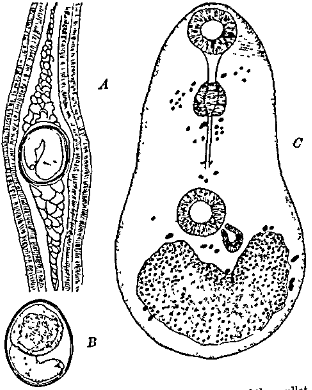

FIG. 110—Metacercaria of *Heterophyes heterophyes* from flesh of the mullet, *A*, cyst between muscles, *B*, cyst dissected out of the flesh, *C*, excysted metacercaria Enlarged. (After Khalil, Journal of Helminthology)

and the cercaria is a lophocercous "eye-spotted" larva. On escaping from the snail this larva attacks the mullet, *Mugil cephalus,* as well as *Tilapia nilotica,* in which fishes it encysts. The encysted metacercaria (Fig. 110 *A, B*) is coiled upon itself. When liberated from the cyst capsule (Fig. 110 *C*), it bears a resemblance to the adult fluke with respect to the shape of its body, the scaly integument and the presence of a genital sucker.

Epidemiology.—Infection of the mammalian host is brought about by consumption of the raw flesh of the mullet and other species of fish Although the mullet is essentially a fresh-water fish, at the spawning season it is caught in salt water. The mullet, as well as a species of *Acanthogobius,* are responsible for the infection in Japan, where, according to Asada (1928), this fluke uses a brackish-water snail, *Cerithidia cingula alata* (*Tympanotonus microptera*), as the first intermediate host. The cercaria migrates to, and encysts in, the fish while in salt- or brackish-water.

Pathogenesis, Pathology and Symptomatology.—Khalil (1934) states that patients harboring pure infections of *Heterophyes heterophyes* suffer primarily from colicky pains and diarrhea, usually have a significant eosinophilia but no anemia.

Diagnosis.—Made on finding the characteristic eggs in the patient's feces. These eggs must be differentiated from other heterophyid eggs, as well as those of *Clonorchis sinensis* and species of *Opisthorchis.*

Therapeusis.—These worms are readily evacuated by administration of carbon tetrachloride, tetrachlorethylene, oil of chenopodium, etc. (For methods of administration, contraindications, etc., see Chapter XXXVI, pp. 641–661.)

Prognosis.—Usually good.

Control.—In Egypt the water containing infected fishes is polluted by the fishermen, who serve as the principal definitive hosts. Salted mullets are the main source of infection. Thorough heating of this fish before its is consumed would prevent infection in man.

Heterophyes katsuradai Ozaki and Asada, 1925.

Genus Metagonimus Katsurada, 1912

(genus from *μετά*, posterior, and *γόνιμος*, genitalia)

Metagonimus yokogawai Katsurada, 1912. (Yokogawa's fluke.)

Synonyms.—*Heterophyes yokogawai* Katsurada, 1912; *Loxotrema ovatum* Kobayashi, 1912, *Tocotrema yokogawai* Katsurada, 1912; *Metagonimus ovatus* Yokogawa, 1913; *Yokogawa yokogawai* Leiper, 1913; *Loossia romanica* Ciurea, 1915; *Loossia parva* Ciurea, 1915; *Loossia dobrogiensis* Ciurea, 1915; *Loxotrema ovatum* Kobayashi, 1908 (*erratum*) of Leiper, 1922.

Historical and Geographical Data.—*Metagonimus yokogawai* of Katsurada, June 30, 1912, was first described as *Heterophyes yokogawai* Katsurada, May 31,

1912, antedating the name *Loxotrema ovatum* Kobayashi, October 10, 1912. (*Loxotrema* preocc. [*Loxotrema* Gabb, 1868 Mollusca].) *Metagonimus ovatus* Yokogawa 1913, although originally intended to designate a different species, is also synonymous with *M. yokogawai* (Kats.).

Metagonimus yokogawai is the common heterophyid fluke of the Far East (Japan, Korea, South Manchuria, Central, West and South China, Formosa and Maritime Provinces of the U. S. S. R.), the Northern Provinces of Siberia, and the Balkan States. It has also been reported from man in Spain (Lopez-Neyra and Pozo, 1932.) First described by Katsurada, from material obtained by Yokogawa from man (Formosa, 1911), and from experimental infection (1911) of dogs and cats with cysts from infected trout (*Plectoglossus altivelis*), and later by Kobayashi (1912) from Korea, and by Ciurea (1915) from Roumania, this species has been referred to under a variety of names. According to Yokogawa (1922), the cyprinoid fishes, *Odontobutis obscurus* and *Salmo perryi*, are also piscine intermediate hosts. Kobayashi (1934) states that the encysted metacercariæ commonly reside in the tissue under the scales and within the fins, rarely in the muscles. The adult worm lives attached to the intestinal mucosa of man, the dog the cat, the pig, the mouse (experimental) and of the pelican (*Pelicanus onocrotalus*.)

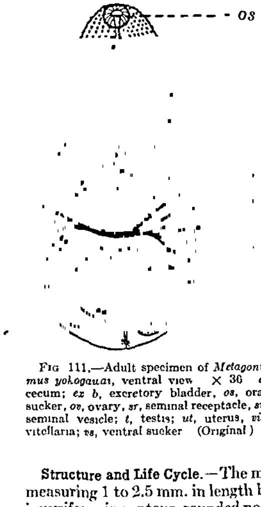

FIG 111.—Adult specimen of *Metagonimus yokogauai*, ventral view × 36 *c*, cecum; *ex b*, excretory bladder, *os*, oral sucker, *ov*, ovary, *sr*, seminal receptacle, *sv*, seminal vesicle; *t*, testis; *ut*, uterus, *vit*, vitellaria; *vs*, ventral sucker (Original)

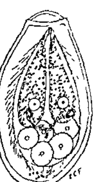

FIG 112—Egg of *Metagonimus yokogawai*, showing internal organization × 1300 (Original)

Structure and Life Cycle.—The mature trematode (Fig. 111) is very small, measuring 1 to 2.5 mm. in length by 0.4 to 0.75 mm. in breadth. The body is pyriform in contour, rounded posteriorly and tapering at the anterior end, and is provided with a complement of integumentary scales The acetabulum, which varies from 66 to 165 μ in length by 55 to 114 μ in width, is deflected to the right of the mid-line, with its long axis directed diagonally. The oral sucker measures 48 to 110 μ in diameter. It leads into a short prepharynx followed by a globose pharynx (29 to 63 μ in trans-section),

then an esophagus, which gives rise to a pair of intestinal ceca ending in the posterior region of the body.

The excretory bladder is tubular, with antero-lateral cornua leading up to the proximal ends of the lateral collecting tubules.

The testes lie somewhat obliquely in the posterior part of the body. They are subglobose and are either entire or slightly lobed in outline. Vasa efferentia, arising from the anterior border of the testes, proceed anteriorwards, uniting to form the vas deferens, which expands into the seminal vesicle, the latter being somewhat retort-shaped and lying transversely from left to right. The vesicula, in turn, leads into the ejaculatory duct, which is surrounded by prostate glands, and opens, along with the metraterm, into the genital atrium. The genital atrium, together with the acetabulum, opens into a pit at the anterior border of the latter. The whole acetabulo-genital apparatus is provided with a complex muscular wall.

The ovary is a globose body about the size of the testes, situated in the mid-plane at the anterior margin of the posterior half of the body. Just behind it and slightly to the left lie the retort-shaped receptaculum seminis and Laurer's canal. The oötype and its enveloping Mehlis' gland are situated to the left of the ovary. The vitellaria are coarse and are arranged in a fan-like distribution in the postero-lateral fields. Collecting ducts assemble towards a common center just behind the oötype, which they

a single vitelline duct.

cecal field and opens

The eggs (Fig. 112)

ures, measuring 26.5

to 28 μ in length by 15.5 to 17 μ in transverse diameter. The opercular shoulder is inconspicuous These eggs can be differentiated from those of *Heterophyes* only with the greatest difficulty. When laid they contain fully mature miracidia, which have a bilaterally symmetrical arrangement of their internal organs

The important first intermediate host of this fluke in Japan, Korea and South China is *Melania* (*Semisulcospira*) *libertina;* in the Yangtze valley, China, *M.* (*S.*) *ebenina;* in Korea, *M.* (*S.*) *extensa*, *M.* (*S.*) *gottschei* and *M.* (*S*) *nodiperda* var. *quinaria*, and in Formosa, *M.* (*Tarebia*) *obliquegranosa* The molluscan hosts are not recorded for the endemic foci in Manchuria, the Amur River and Maritime Provinces of the U. S. S. R., the Bal'

(fir

red

from the snail (Fig. 114) have an oblong body, attenuated at the anterior end, and are provided with a long, lophocercous caudal organ having dorsoventral flutings The body proper is covered with spines. The acetabulum is situated under the excretory bladder, its muscular elements being poorly developed. In the anterior third of the body, on the dorsal aspect, there is a pair of pigmented "eye-spots" In the vicinity of these "eye-spots" there are aggregations of golden-brown granules, while posteriad from each "eye-spot" there is a streak of such granules The entire subintegumentary layer of the body is also more or less suffused with these pigmented granules,

The anterior end of this cercaria, like that of the cercariæ of other members of the family **Heterophyidæ**, is provided with a peculiar armament. The oral sucker is anterior in position with its opening slightly ventral. Surrounding the opening are several circlets of strong hook-shaped spines which can be readily distinguished from the smaller integumentary spines. Immediately in front of the oral opening (Fig. 114 *A*) are two alternating rows of spines. Projecting from the oral opening is a scoop-like "chitinous lip," with minute needle-like processes on its incomplete dorsal margin. Some seven pairs of penetration glands occupy the middle of the body. Ducts from these glands ascend anteriad and, after passing through the roof of the oral sucker, open through reinforced capillary tubules anterior to it (Fig. 114 *A*, *B*). Within the oral sucker is a short prepharynx, a small

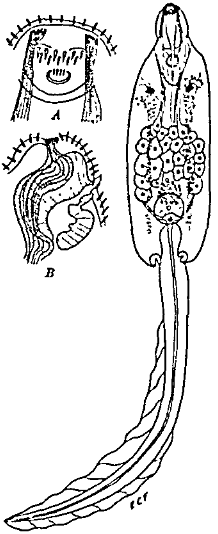

FIG. 114.—Cercaria of *Metagonimus yokogawai*. × 200. *A*, *B*, ventral and lateral views of anterior end showing relationship of penetration ducts and integumentary spines to oral opening, greatly enlarged. (Craig and Faust, adapted in part from Faust, 1929, in part from Yokogawa, 1931.)

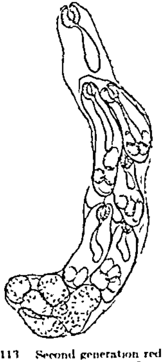

FIG. 113. Second generation rediæ of a heterophyid fluke developing in first generation redia. (Drawing by Yokogawa.)

globose pharynx and a long esophagus. The ceca are masked by the penetration glands. The excretory bladder is triangular in shape and has a pair of lateral collecting tubules and an unpaired caudal one emptying into it.

The cercaria, on emerging from its molluscan host, first swims about vigorously through the water, but on finding an appropriate fish in the

vicinity, attacks it and penetrates under the scales and into the flesh, utilizing penetration gland secretions to digest the host tissue. The common edible, fresh-water fishes which are sources of human infection for this fluke in Japan are *Plectoglossus altivelis* and *Leuciscus hakuensis*. On entering the fish, if not before, the tail of the cercaria is discarded. Once within the flesh of the fish or, at times, even under the scales, the larva secretes a cystogenous fluid which "sets" in the form of a more or less spherical membrane around it. The presence of the parasite in the host tissue also stimulates a host-tissue reaction, resulting in the formation of the false outer capsule. The encysted larva grows more or less, depending on the food supply in the immediate vicinity as well as upon the duration of its period of encysted life.

Epidemiology.—On consumption of the infected raw fish-flesh, man and other mammals (or birds) become infected The outer cyst wall is digested away as the food mass passes through the stomach. The inner membrane serves as a safeguard for the parasite until it reaches the duodenum, where the membrane is weakened by the intestinal juices and the activated larva breaks through the membrane, attaches itself to the intestinal mucosa and develops to adulthood.

Other Heterophyid Parasites of Man.—Probably all members of the family Heterophyidæ are potential parasites of the human intestine. In Nature and/or by experimental tests the following species have been reported from man: *Heterophyes brevicæca* Africa and G
cestus armatus (Tanabe, 1922) and *C. for*
Japan and Formosa respectively; *Meta*
(Formosa); *Haplorchis pumilio* (Looss, 1896) (syn. *Monorchotrema taihokui* Nishigori, 1924), the Philippines and Formosa, *H. yokogawai* (Katsuta, 1932), the Philippines and Formosa, *H. taichui* (Nishigori, 1924), the Philippines and Formosa; *H microrchia* (Katsuta, 1932), Formosa; *Diorchitrema pseudocirratum*
of Onji and Nishio, 1916 (?)),
(Katsuta, 1932), Formosa,
They all involve species of *Melania* (*sensu lato*) as first intermediate hosts. *C. formosanus* utilizes *Melanoides tuberculatus* var. *chinensis*; *H. pumilio*, *Semisulcospira libertina* var. *hidatchiens* in Formosa, *H. taichui*, *Tarebia obliquegranosa* in the Philippines, and *D. formosanum*, *S. libertina* var. *subplicosa* as well as *T. obliquegranosa* in Formosa. Fishes are the usual second intermediate hosts Moreover, Chen (1944) has reported natural infection of *Rana limnocharis* and *Bufo melanostictus* with metacercariæ of *Haplorchis* and *Centrocestus* in the vicinity of Hongkong, and Vasquez-Colet (1943) claims to have found young shrimp of the genus *Penaeus* infected with the metacercariæ of *Haplorchis yokogawai*. Infection of the definitive host is acquired through consumption of raw infected second intermediate host. Alicata (1937; 1949, personal communication) has found *D. pseudocirratum* in native Hawaiians, contracted from eating local mullet.

Pathogenesis, Pathology and Symptomatology of Infections with Species of the Family Heterophyidæ.—The two species of this family which occur as common parasites of the intestinal tract of man and reservoir hosts,

Heterophyes heterophyes and *Metagonimus yokogawai*, as well as the other species listed above, which have been occasionally recorded from man, all produce essentially similar lesions in the intestinal wall. The flukes deeply invade the mucous membrane (Fig. 115), where they become attached by their suckers. At times many eosinophils and leukocytes are seen in the mucous membrane, but no marked pathological change is usually recognizable. The intestinal epithelium may become slightly atrophied and wide stretches of solitary intestinal glands are occasionally seen. Some flukes, which have invaded the mucous membrane, again come to lie with their heads attached to the surface of this layer. On the whole, the pathological changes due to the presence of these worms in the bowel wall are slight, and symptoms due to their presence are usually negligible. In cases of heavy infection, mild digestive disturbances may result and even severe, persistent diarrhea may develop if extensive stretches of the mucosa are involved. Alicata and Schattenburg (1938) have attributed a severe diarrhea in a Japanese patient in Hawaii to a heavy infection with *Stellantchasmus falcatus*, acquired from eating raw mullets.

In the Philippines, where Africa and his associates (1935, 1936, 1937) have made a careful study of heterophyid infections in man (species of

FIG 115.—Section of ileum, showing position of heterophyid fluke among the villi × 100 (After Faust and Nishigori, Journal of Parasitology.)

Heterophyes, *Haplorchis*, *Diorchitrema*, etc.), serious sequelæ have been discovered, so that these workers designate the worms as "decidedly pathogenic." At times the eggs, laid by the worms, filter through the intestinal wall into the lymphatics and pass through in massive numbers into the general circulation. They may be filtered out in the blood vessels of the myocardium or in the valves, where cellular reaction initiated by their presence results in cardiac failure, with an associated syndrome superficially resembling beriberi. Or they may be carried to the spinal cord and brain, where they set up grave pathological processes, indicative of loss of function of the motor and sensory neurons of the involved areas. Manalang (personal communication, 1948) confirms the finding of heterophyid eggs in ectopic foci but states he has been unable to demonstrate the causal relationship of the eggs to the diseased states.

Faust and Nishigori (1925) have shown that the heterophyid flukes upon

excystment in experimental dogs first become attached to the intestinal mucosa in the region of the jejunum, where they grow to adulthood. In the course of time, as they release their hold on the mucosa, they become gradually extruded into the lumen of the intestine, along with mucus and other exudates, usually securing a hold farther down In this way they become attached farther and farther distad, eventually reaching a location where residence is no longer tenable, whereupon they are evacuated in the feces. Thus spontaneous expulsion eventually results, so that the body is free from these flukes, provided reinfection does not occur. On the other hand, Africa (1937) states that evidence is accumulating, favoring the view that worms, which *actually invade the intestinal mucosa* and mature there, remain in these sites until they die Moreover, "the very mild tissue reaction observed around the worms in the intestinal wall and the general absence of attempts to encapsulate the parasite by fibrosis may account for the filtration of eggs into the general circulation observed in human cases."

These parasites are relatively common in the human population in Egypt (*Heterophyes heterophyes*) and in parts of the Far East (*Metagonimus* et al.).

Diagnosis.—This is made upon finding the eggs of these flukes in the f

to a champagne hue.

They vary in size from 20 to 35 μ in length by 11 to 20 μ in width, depending on the species. Each egg has within its shell a bilaterally symmetrical larva, well developed at the time the egg is laid. The eggs of these flukes are frequently confused with those of *Clonorchis sinensis* (27 to 30 by 15 to 17 μ) and *Opisthorchis felineus* (30 by 11 μ), the two latter, however, po the internal organs of the larva.

ood evidence that in the course of e spontaneously evacuated from he entry of the eggs into tissues of the heart and of treating all infected persons as soon as they are diagnosed. Carbon tetrachloride, tetrachlorethylene, or any anthelmintic satisfactory for the removal of hookworms, or the recommended

Prognosis —

been deposited in the heart tissues or central nervous system.

Control.—Infection in man may be prevented by thoroughly cooking all fresh-water and salt-water fish to be consumed.

Superfamily Troglotrematoidea Faust, 1929, Emend, 1939

This superfamily contains only members of the family **Troglotrematidæ**.

Type Family TROGLOTREMATIDÆ Odhner, 1914

This family comprises a few species of distomes of which the relationship to other groups is relatively remote. The flukes are small to moderate-

sized trematodes, ovate in contour, nearly circular in cross-section, with poorly developed musculature and well-developed genital organs. The only members of the family parasitic in man are *Troglotrema salmincola* and *Paragonimus westermani.*

Genus Troglotrema Odhner, 1914

(genus from τρώγλη, sunken, and τρύμα, orifice)

Troglotrema salmincola (Chapin, 1926) Witenberg, 1932.

Synonyms.—*Nanophyes salmincola* Chapin, 1926; *Nanophyetus salmincola* Chapin in Hall, 1927; *Nanophyetus schikhobalowi* Skrjabin and Podjapolskaja, 1931.

This is the trematode associated with "salmon-poisoning" of dogs on the Pacific Coast of North America. It has been recorded from the coyote (*Canis lestes*), the fox, the mink, the raccoon (*Procyon psora pacifica*), the lynx (*Lynx fasciatus fasciatus*) and from aborigines in Eastern Siberia.

The worms (Fig. 116), which *per se* are apparently relatively nonpathogenic, are small, pyriform objects, somewhat flattened dorsoventrally, measuring 0 8 to 1.1 mm in length by 0.3 to 0 5 mm in breadth. The oral sucker measures 0 15 to 0.18 mm. in diameter, while the ventral sucker, situated near the midventral position, is 0.12 to 0.13 mm. in diameter. Within the oral sucker, a pharynx (60 μ in length) leads into an esophagus of equal length. The distended ceca extend posteriad to approximately the middle plane of the testes. There ... -side large, vesi- cker, to the left of the rounded ovary. There is a Laurer's ... has been observed. The blad- The vitellaria are composed of numerous discrete follicles, extending dorsally from the plane of the esophagus to the posterior end of the worm The genital sinus lies just posterior to the ventral sucker The eggs, which are present in scanty numbers in the uterus, are broadly ovoidal, operculate objects, are relatively thick-shelled, yellowish in color, and measure 60 to 80 μ by 34 to 50 μ.

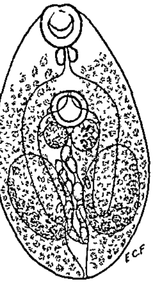

Fig. 116.—Adult specimen of *Troglotrema salmincola*, ventral view × 160. (After Witenberg, Jour. Parasitol., courtesy of Am. Soc Parasitol)

The appropriate molluscan hosts in Oregon and elsewhere in the Pacific Northwest of the United States are *Galba plicifera plicifera* and *G. plicifera silicula*. The cercaria, which develops in a redia, measures 270 by 80 μ, has a simple stylet, six ... tail The free-swimming cercariæ become ... out. When eaten ... finitive host ... is (Simms, 1932), ... h containing the encysted metacercariæ. In dogs, coyotes and ... agent produces a severe, frequently fatal infection. There is an incubation period of six to ten days, followed by a sudden onset of symptoms, with complete loss of appetite, rise in temperature and marked depression of the sensorium. There is a purulent discharge

from the eyes, with edema. From the fourth day vomiting is practically uncontrolled, especially after drinking water. The stool becomes dysenteric. Meanwhile the temperature drops to normal or subnormal. In the latter case death frequently ensues. Thus far this disease syndrome has not been recorded from man.

If the disease is diagnosed at its onset, the oral administration of apomorphine (2 to 6 mgs.) within the first three hours will protect the infected animal. For the fluke infection in man Strom (1935) states that *filix-mas* is an efficient anthelmintic.

Genus Paragonimus Braun, 1899

(genus from παρά, side-by-side, and γόνιμος, gonads)

Paragonimus westermani (Kerbert, 1878) Braun, 1899 (The Oriental lung fluke, causing paragonimiasis, pulmonary distomiasis or endemic hemoptysis.)

Synonyms.—*Distoma westermani* Kerbert, 1878, *D. ringeri* Cobbold, 1880; *D. pulmonum* Baelz, 1880; *D. pulmonis* Kiyona, 1881, *D. fusca* Baelz, 1881; *D. pulmonale* Baelz, 1883; *D. baelzi* Cobbold, 1884; *D. westermani* Leuckart, 1889, *D. cerebrale* Yamagiwa, 1890; *Mesogonimus westermanii* Railliet, 1890, *Polysarcus westermannii* Lühe, 1899; *Paragonimus compactus* (Cobbold, 1859); *P. edwardsi* Gulate, 1926 (?); *P. ohirai* Miyazaki, 1939 (?)

Historical Data.—*Paragonimus westermani*, the Oriental lung fluke, was discovered by Kerbert in 1878 in the lungs of two Bengal tigers which had died in the Hamburg and Amsterdam zoological gardens. In 1879 a Portuguese resident of Formosa died of rupture of an aortic aneurysm and, on autopsy by Ringer, was found to have in his lungs a parasite, which was forwarded to Manson in Amoy and recognized by him as a distomate fluke. A year later Manson found large operculate eggs in the rusty, blood-flecked sputum of a Chinese patient who had lived in Northern Formosa. Finding these eggs to be similar to those expressed from Ringer's fluke, he sent the material to Cobbold, who pronounced it a new trematode and named it *Distoma ringeri* (1880). Meanwhile, Baelz (1880) had found trematode eggs in the sputum of hemoptysic patients in Japan, and in 1883 recovered the

and fresh-water crustaceans, has been elucidated by Nakagawa, Miyairi, Yoshida, Ando, Yokogawa and Kobayashi for Japanese territory, and more recently by Vogel, Wu and Watt (1935), and Chen (1937) for Chinese endemic areas.

In 1940 Chen created a new species, *P. iloktsuenensis*, for the lung fluke he had recovered from the brown rat (*Rattus rattus caracao*) and the black rat (*R. rattus flavipectus*) of the Canton area, China. Previously (1935–1937) he had regarded this parasite as *P. westermani*. Tang (1940) has found this rodent lung fluke in Fukien Province, China.

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Yucatan and other states of Mexico have also been reported, apparently erroneously,

as having autochthonous cases. Meira, Correa and Melo Albuquerque (1943) have provided convincing evidence that no indigenous cases of paragonimiasis have been discovered in Brazil and that textbook references to its presence in the State of Matto Grosso have perpetuated an error originating with Diesing (1850).

Stoll (1947) has estimated that the world incidence of human paragonimiasis is 3.2 millions, almost exclusively in the eastern part of Asia and adjacent islands.

Ward and Hirsch (1915), Vevers (1923) and Khaw (1930) have favored the view that *Paragonimus westermani* (Kerbert, 1878) and *P. ringeri* (Cobbold, 1880) are distinct species. Their conclusions are based partly on differences in the integumentary spines and in the shape of the eggs, and partly on the grounds that human cases are rare in Bengal and other parts of India, where the lung fluke is commonly found in members of the cat family. Kuang Wu (1938) states that "the cuticular spines of the lung fluke afford poor criteria for distinguishing the species." Thus far reciprocal life history tests have not been reported.

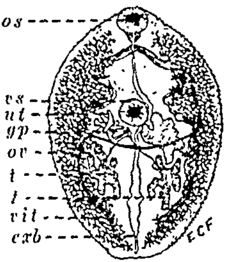


FIG. 117.—Adult specimen of *Paragonimus westermani*, ventral view. × 5. *ex b*, excretory bladder; *gp*, genital pore; *os*, oral sucker; *or*, ovary; *t*, testis, *ut*, uterus, *vit*, vitellaria; *vs*, ventral sucker (Original adaptation from Leuckart, Parasiten des Menschen.)

Structure and Life Cycle.—*Paragonimus westermani* (Fig. 117) is a plump, ovate fluke, abruptly rounded anteriorly and slightly more tapering posteriorly, measuring 7.5 to 12 mm. in length by 4 to 6 mm. in breadth by 3.5 to 5 mm. in thickness. Worms, freshly obtained, are reddish-brown; preserved specimens are gray. The integument is provided with scale-like spines, arranged in groups encircling the worm. These spines may be entire or toothed. The acetabulum,

... The oral sucker, with a diameter of 0.75 mm., is subterminal. It lead through a short prepharynx into a globose pharynx (0.3 mm. in trans-section), followed by a short esophagus, which bifurcates to form the somewhat meandering ceca, the latter extending to the subcaudal region of the body.

The excretory pore is slightly ventral in position. The bladder is a long, convoluted pouch, reaching from the posterior extremity anteriad to the plane of the pharynx. The lateral collecting tubules arise from the bladder somewhat behind the ovary, proceed laterad and branch into anterior and posterior stems, each with numerous secondary and tertiary twigs.

The testes, which are irregularly lobed organs, are situated slightly obliquely in the posterior third of the body. From the center of each testis there arises a vas efferens. The two vasa run anteromesad and in the vicinity of the oötype unite into the vas deferens. The latter is a broad tube lying obliquely in a dorso-ventral position; it constitutes the vesicula seminalis. At its outer extremity it is modified into the pars prostatica, followed by the ejaculatory duct. As the ejaculatory duct approaches the ventral surface, it unites with the metraterm, to empty through a common

tubule into the genital atrium. A cirrus pouch is lacking The genital pore lies behind the acetabulum and slightly to the right of the mid-line.

The ovary is a lobed organ, slightly larger than the testes, and is situated behind and somewhat to the left of the acetabulum (*i. e*, to the observer's right). From its posterior aspect there arises an oviduct, which proceeds dorsad and enters theof Mehlis' gland complex. *En route* the oviduct is joined with an out-pocketing, consisting of a small receptaculum seminis, with its delicate convoluted tubule (Laurer's canal), which opens on the dorsal surface of the worm. Th

of the pharynx to the posterior end of the worm On piercing Mehlis' gland the common female duct becomes transformed into the ootype,

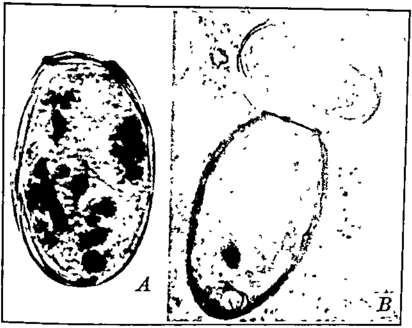


FIG 118 —Photomicrographs of eggs of *P westermani* *A* egg discharged in sputum, × 666, *B*, miracidium hatching from egg, × 580 (*A* after Faust, in Brennemann's Practice of Pediatrics, courtesy of W F Prior Company *B*, original photograph courtesy of O K Khaw)

which has a general dorsoventral position The uterus arises from the ventral end of the oötype, proceeds across to the right side of the body and in the region postero-dextral to the acetabulum is knotted into several coils, finally emerging on the inner side as the metraterm and uniting with the ejaculatory duct to enter the genital atrium.

The eggs of *Paragonimus* (Fig. 118) are broadly ovoidal objects with a distinct operculum at one end inserted into a slightly thickened collar region, and with a thickening of the shell at the abopercular end. They are golden-brown in color and measure from 80 to 118 μ in length by 48 to 60 μ in cross-section The maximal width is nearer the operculum than the equator of the egg. The freshly laid egg is immature and contains an

abundance of heavy yolk cells. The eggs are voided into the cystic pockets around the worms, and on rupture of these pockets, or through the eroded bronchiolar connections within the cyst, the eggs escape. They are most commonly recovered from the sputum, which has a characteristic rusty-brown tinge when they are present. In about 40 per cent of the cases they are also found in the feces. The eggs require from sixteen days to several weeks for complete development, whereupon they hatch and the miracidia, escaping into the water, swim about in a vigorous fashion. Watanabe (1935) states that the epithelium of the larva consists of 17 cells, arranged in four rows. The miracidium has an apical cone, a pair of sense organs, a

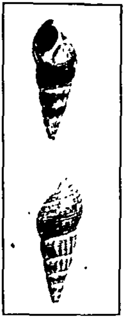


FIG. 119

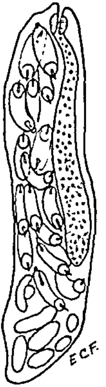


FIG. 120.

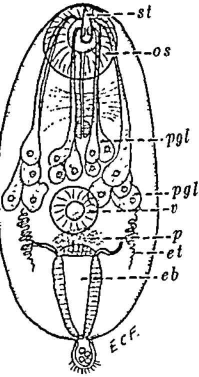


FIG. 121

FIG. 119.—*Melania (Semisulcospira)* ... of *Para-gonimus westermani* in the Far East. N ... t

FIG. 120.—Second generation redia o ...
× 67. (Adapted from Tang, Chinese Med. Jour., 1940.)

FIG. 121.—Cercaria of *P. westermani* from Fukien Province, China. *eb*, excretory bladder; *et*, excretory tubule, *os*, oral sucker, *p*, genital primordia; *pgl*, penetration gland, *st*, stylet; *v*, ventral sucker. × 300. (Adapted from Tang, Chinese Med. Jour. 1940.)

pair of flame-cells and convoluted excretory tubules. "Eye-spots" are lacking. Upon coming in contact with the appropriate mollusc the miracidia attack and penetrate its soft tissues. *Melania (Semisulcospira) libertina* (Fig. 119) is the most widely distributed snail involved as first intermediate host (Chekiang, Fukien, Hunan, Hupeh and Yünnan Provinces of China, Korea, Formosa). The following snails have also been found naturally infected: *M. (S.) extensa* (Japan, Korea); *M. (S.) paucicincta* (Japan, Korea); *M. (S.) nodiperda* and var. *quinaria*, *M. (S.) gottschei*, *M. (S.) libertina* var. *hidatchiens* and *M. (S.) multicincta* (Korea); *M. (S.)*

toucheana (Fukien Province, China); *M.* (*Tarebia*) *obliquegranosa* (Formosa), and *Assiminea lutea* (Canton and possibly Anhwei Province, China). The record of *Melanoides tuberculatus* for Formosa is possibly one of misidentification of the parasite. *Ampullaria luteostoma* is said to be involved in Venezuela, but this requires verification, since this mollusc is only distantly related to the optimum hosts in endemic areas in the Far East. According to Tang (1940) the rodent lung fluke in Fukien Province, China utilizes a rissoid snail, *Oncomelania nosophora tangi*.

On entering the mollusc the miracidia cast off their ciliated epithelium, become transformed into globular or ellipsoidal sporocysts and produce the first generation rediæ. These rediæ escape from the mother sporocysts, wander farther up the lymph spaces of the mollusc and, after reaching the lymph sinuses around the digestive gland, produce a second generation of rediæ (Fig. 120). These, in turn, produce the cercariæ, about twenty of which may be seen at one time in all stages of development. These larvæ (Fig. 121) are microcercous forms, with an ellipsoidal body and a short knob-like caudal [illegible] s, posteriorly directed spines [illegible] 70 to 80 μ in breadth. The i [illegible] spines, which are seldom seen in preserved material. The acetabulum is relatively small (*ca* 30 μ in diameter), and the oral sucker disproportionately large (*ca* 57 μ in diameter). Inserted in the dorsal wall of the oral sucker is a simple cone-shaped stylet. Within the oral opening there is a relatively long, delicate prepharynx, leading into a small pharynx and thence into a rather indistinct esophagus. The ceca are rarely distinguishable. The bladder is ovoidal to trigonate, has a thick wall and opens subterminally. There are two types of penetration glands opening through individual ducts at the sides of the stylet. These consist of four pairs of larger, deeply staining, lateral glands, and three pairs of somewhat smaller, lightly staining, med [illegible] tuated in the middle of the [illegible] ed. Several weeks are req [illegible] e life cycle.

On erupting from the molluscan host, the cercariæ of *Paragonimus* swim around in the water and, in the event a crayfish or appropriate crab is in the immediate vicinity, swarm around these crustaceans and penetrate their soft parts, where they secrete cystogenous fluid and encyst. The following species of crustacean hosts have been found naturally infected in the Sino-Japanese areas: The crayfishes, *Astacus* (*Cambaroides*) *japonicus* (Fig. 122 *A*) and *A. similis*, the crabs, *Eliocheir japonicus*, *E. sinensis*, *Potamon dehaani* (Fig. 122 *B*), *P. rathbuni* (*P. obtusipes* of parasitologists), *P. denticulatus*, *Parathelphusa sinensis*, *P.* (*Barythelphusa*) *mistio* (Luzon, P. I., Tubangui, 1947), *Sesarma dehaani*, and *S. sinensis*. *Pseudothelphusa iturbei* has been incriminated in Venezuela The cysts (Fig. 123) are spherical, pearly-white objects, found in practically all the soft parts of the crustacean host, but can be most readily detected in the gill filaments,[1] although Vogel, Wu and Watt (1935) have found them more abundant in the muscles of the thoracic legs than in the gills or liver. They lie encapsu-

[1] Cysts of *Paragonimus* must not be confused with other species of encysted flukes commonly found in the liver of crustaceans

lated in an outer host-tissue envelope. They are apparently able to increase in size, depending on the abundance of food supply with which they are surrounded. The definitive host is infected from eating the raw soft parts of fresh-water crabs or crayfishes infected with the cysts, and, to a lesser extent, perhaps, by the ingestion in drinking water of cysts that have become free from their crustacean host. In the Chekiang endemic area of China the living crabs are placed in rice wine or brine solutions along with condiments. Later the soft parts are sucked out by the feaster. Although the crab itself is dead, the encysted metacercariæ are still viable.

On entering the stomach of the mammal, the cyst is digested out of the surrounding tissue and the outer (false) tissue capsule is then digested off. Upon arrival in the duodenum, the true cyst wall is weakened so that the metacercaria emerges, whereupon, according to the investigations of Yokogawa and of Kuang Wu (1938), it penetrates through the wall of the small intestine, traverses the abdominal cavity, whence it migrates upwards

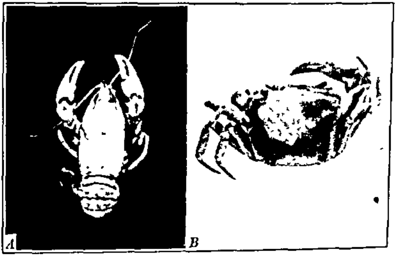


FIG. 122. Second intermediate hosts of *Paragonimus westermani*. *A*, *Astacus japonicus*, *B* *Potamon dehaani* Natural size (Original photographs)

through the diaphragm to the thoracic cavity, penetrates through the pleura into the lungs and finally arrives in the bronchioles, where it settles down and becomes pocketed off by a cystic capsule resulting from the infiltration of host tissue cells. Here the worm grows to adulthood.

Localization of the flukes in the lungs is apparently the most usual outcome of the migration of the metacercariæ, although it is not necessarily obligatory, since the worms are at times found in foci far removed from the respiratory tract, such as the various lymph spaces in the body, the ventricles of the brain, the orbit, and muscles of the extremities. The period of migration and development within the definitive host usually occupies several weeks.

Paragonimus kellicotti Ward, 1908 has a distribution limited to North America. It is most commonly a parasite of the mink (*Mustela vison*), but has also been found in the pig, dog, muskrat, oppossum (*Didelphys virginiana*), cat, wild cat, goat, and once probably in man. The known distribution includes the following states: Michigan, Wisconsin, Minnesota,

Ohio, Indiana, Illinois, Iowa, Pennsylvania, Virginia, West Virginia, Kentucky, Missouri, Mississippi, South Carolina, Georgia and Louisiana Cameron (*fide* La Ru[illegible] common in the dog ar[illegible] man infection was th[illegible] States for twenty years, during which time his food had been frequently prepared by Chinese cooks.

The first intermediate host of *P. kellicotti* is the snail, *Pomatiopsis lapidaria*, in which the sporocyst and two redia generations develop, and from which the styletted, microcercous cercariæ emerge (Ameel, 1934). Species of the crayfish genus *Cambarus* serve as second intermediate hosts. In these crustaceans the metacercariæ are encysted in the cardiac region. The infected crayfish, when consumed without adequate cooking, produces infection in the mammal. The lungs are the most common site of infection.

Epidemiology.—The natural definitive hosts include man, the tiger, cat, wild cat, leopard, panther, fox, wolf, dog, pig, beaver, wolverine, "pencilled cat" (*Nyctereutes procyonides*), civet cat (*Viverricula indica pallida*), the crab-eating mongoose (*Herpestes urva*) and the Indian mongoose (*Mungos mungo*). Tang (1940) found that in Fukien Province, China the snails and crabs infected with the rodent lung fluke occurred in the slowly moving waters of the flat valleys, whereas the intermediate hosts of *P. westermani* were present typically in the fast-flowing mountain streams of the same general localities. Human infection may result from consumption of frankly raw crabs or crayfish harboring the encysted metacercariæ of this fluke, as among the aborigines of Formosa. More usually, however, it is occasioned by eating the soft parts, including the leg muscles, of these crustaceans which have been previously placed in brine, vinegar or wine, which kill and "cook" the crustacean tissues but do not sterilize the cysts.

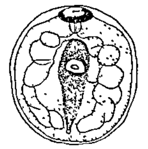


FIG 123 — Encysted metacercaria of *Paragonimus westermani* from the fresh-water crab, *Potamon dehaani* × 500 (After Yokogawa)

Pathogenesis, Pathology and Symptomatology.—*Paragonimus westermani* is normally a resident of the lungs. The metacercaria arrives in the intestine of the host in t[illegible] crab or crayfish [illegible] of migration of [illegible] intestinal wall, then traversing the abdominal cavity, penetrating through the diaphragm into the pleural cavity, entering the lungs and, on arriving in a bronchiole, settling down and developing to adulthood. This complicated path taken by the parasite from the intestine to the pulmonary parenchyma explains why there are so many cases in which the young worms become lodged in ectopic foci Frequently, perhaps in the majority of cases of experimental hosts, the parasites are found in pairs, but in man they usually develop singly.

The presence of these flukes in the lungs provokes a tissue reaction on the part of the host (Fig 124), consisting of a leukocytic infiltration imme-

diately around the parasite and the development of layers of fibrous tissue around the latter, thus constituting a thick adventitious capsule around the invader, and more or less effectively excluding the by-products of the latter from the body of the host. These cysts, which may be superficial but are

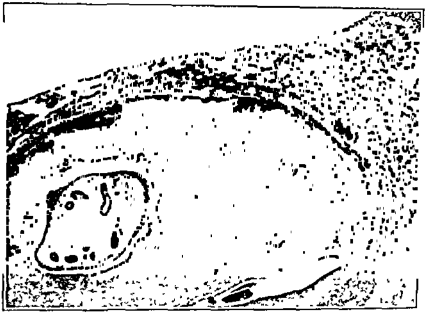


Fig. 124.—Section of lung with *Paragonimus* infection, showing leukocytic infiltration fibrous connective-tissue encapsulation and eggs of the parasite throughout the alveoli (Original, from experimental material presented to the author by Professor S Yokogawa)

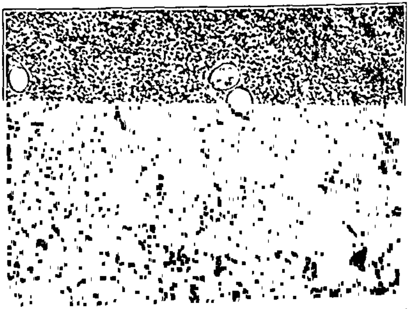


Fig. 125 —Section of abdominal tumor infiltrated with *Paragonimus* [illegible] al from a preparation by Dr A. I. Ludlow)

more commonly formed throughout the deeper tissues of the organ, are usually *the size of a filbert.* Between the capsule and the fluke there is an accumulation of blood-tinged purulent fluid with minute rusty-brown flecks, which are clusters of the eggs of the parasite.

to the peritoneum or pleura, where it may be recognized by the peculiar slaty-blue color of the cyst. In the lungs the cystic pockets housing the worms, if not actually in the bronchi, are usually connected by channels with the respiratory passages and thus discharge their eggs and by-products from time to time into the air passages. Likewise, cysts not opening into the bronchi, as well as those in other tissues of the body, may work their way to a mucous or epithelial surface, such as the intestinal mucosa, biliary tract epithelium, pleural or peritoneal surface, or even the skin, in which foci they may proceed to ulcerate.

Musgrave, who made a careful study of paragonimiasis lesions, recognized four types, namely, (1) the non-suppurative lesion, (2) the tubercle-like lesion, (3) the suppurative lesion, and (4) the ulcerative lesion. The first type consists in the infiltration of the tissue (Fig. 124) by eggs of the fluke, at first provoking no tissue reaction but later producing round-cell or connective-tissue infiltration, eventually leading to abscess-formation and possibly ulceration. The eggs or parasites on serous surfaces may give *rise to adhesive inflammation. In most instances the host tissue attempts* to delimit the process by a fibrous wall, thus producing the typical paragonimiasis lesion, with the parasite and its discharged products in the center, surrounded by a thick fibrous wall and superficially an area of connective tissue. The abscess may at times form caseous material, with a tubercle-like aspect. In the ulcerative type, healing may be attempted but is only partly successful. The infiltration of the eggs into the tissues produces a peppered, rusty-brown appearance, which is frequently visible to the naked eye.

The paragonimiasis lesions in the lungs consist in generalized or localized diffuse cirrhosis, cystic dilatation of the bronchi, pseudo-pneumonia, and tubercle-like abscesses The pulmonary disease is usually insidious in its onset and chronic in its course, but there may be a sudden onset with chills and fever, and fulminating cases with a fatal termination are recorded. Typically there is bronchial cough with the discharge of a viscous, frequently blood-tinged sputum containing flecks of dark golden-brown particles, the eggs of the parasite. Occasionally there is profuse hemoptysis following paroxysmal coughing. Due to this characteristic the disease has been commonly designated as "endemic hemoptysis." The physical signs in this type of the disease may suggest bronchopneumonia or pleural effusion. The abdominal type, in which the lesions may be in the liver, spleen, pancreas, intestines, or on the serous layers, usually produces much vaguer symptoms, with dull generalized abdominal pain, moderate rigidity and tenderness on deep palpation and at times evidence of an abdominal tumor mass.

In the intestinal variety, diarrhea frequently occurs, with eggs in the

ized in the dermis or subcutaneous tissues, they frequently produce abscessing tumors.

The cerebral type is accompanied by a peculiar variety of Jacksonian epilepsy, with eventual symptoms of hemiplegia, monoplegia, aphasia, ocular dysfunction, or paresis. Brain symptoms in children under fifteen years of age in endemic foci in Japan have in the past been commonly *diagnosed as infantile* paralysis, cerebral hemorrhage, encephalitis, or meningitis. Many of these cases also had pulmonary symptoms, with *Paragonimus* eggs in the sputum. The brain syndrome is attributed to *adult or adolescent worms, which had migrated* into the organ and become encysted.

Eosinophils are usually localized around the paragonimiasis abscesses, but, *in case the toxic products of the worm become absorbed by the body*, generalized eosinophilia may result. Under such conditions, complement-fixation is positive and may be used for diagnostic purposes where other methods are not feasible. *Human infection is, for the most part, confined* to the Far East, with certain heavy endemic foci in Japan, Southern Korea, Chekiang and Kweichow Provinces (China), and Formosa.

Diagnosis.—This depends on the *finding* of *Paragonimus eggs* in the body excreta or discharged from cutaneous lesions. In the pulmonary type, eggs can usually be recovered from the sputum, which is tinged a rusty-brown by their presence. Likewise, these eggs occur in the feces of about 40 per cent of patients having only pulmonary symptoms. In the intestinal type with diarrhea, the eggs are usually discharged directly into the intestinal lumen. In other foci of the body diagnosis of the parasite may require postponement until biopsy can be performed and a section of the tissue examined microscopically. Extract of *Paragonimus* adults in physiological salt solution produces a positive complement-fixation reaction with patients' serum, but no hemolytic property of the worm has been *demonstrated*. Ando (1921) believes that infection confers partial immunity. Clinically the pulmonary type needs to be differentiated from bronchopneumonia, tuberculosis, bronchospirochetosis and pleural effusion. *The intestinal* type requires differentiation from the intestinal schistosomiases. *The* diffuse abdominal type is perhaps the most difficult to diagnose. The [illegible] epilepsy or [illegible] pulmonary paragonimiasis there are shadows of [illegible] are concrete diagnostic evidence of the disease. A history of the patient having resided *in* endemic areas frequently aids in diagnosis.

Therapeusis.—Cases treated with emetine or tartar emetic are temporarily relieved of pulmonary symptoms. Yokogawa (1939, 1940) found emetine and prontosil in combination to be moderately effective in controlling the disease. Meira, [illegible] total of 0.56 Gm. of [illegible] period of fourteen days to a Japanese patient in Brazil who [illegible] from pulmonary paragonimiasis. They noted an *ameliorization* of symptoms accompanied by the evacuation of *abnormal* eggs and then their complete disappearance from the sputum. The author observed the clinical usefulness of emetine hydrochloride *in* the treatment of two natives of

Mindanao, P. I. treated in an American Army Hospital in 1945. In these patients the pulmonary lesions had opened into the pleural cavity, with eggs of *P. westermani* in a thick purulent liquid obtained by aspiration. Following treatment the eggs disappeared from the aspirate and the effusion then cleared up. Whenever feasible, removal of the patient from endemic areas is recommended. After five or six years such individuals frequently recover from clinical symptoms.

Prognosis.—Fair, except in heavy infections or in individuals where the parasite is localized in primary centers such as the brain. Pulmonary paragonimiasis associated with tuberculosis of the lungs usually has a poor prognosis.

Control.—The disease may be prevented by abstinence from eating raw, freshly salted, pickled or inadequately cooked fresh-water crab or crayfish meat. Since immersion of the infected crustacean host in rice wine or strong brine will not kill the cysts of this fluke, it is imperative that the crayfish or crab be prepared in a bisque, fried in deep fat, or otherwise thoroughly heated, in order to guarantee safe consumption.

SUPERFAMILY HEMIUROIDEA FAUST, 1929, EMEND. 1939 (SYN. HEMIURIDA DOLLFUS, 1923)

This superfamily contains those species of distomate flukes with a Y-shaped excretory bladder, which have cystophorous cercariæ. These cercariæ gain entrance to a copepod second intermediate host, where they live unencysted in the body cavity of that host. The adults are normally parasitic in lower vertebrates.

Family ISOPARORCHIIDÆ Poche, 1926

GENUS, ISOPARORCHIS SOUTHWELL, 1914

(genus from ἴσος, equal, παρά, side-by-side, and ὄρχις, testis)

Isoparorchis hypselobagri (Billet, 1898).

Synonyms.—*Leptolecithum trisimilitubis* Southwell, 1914; *Leptolecithum eurytremum* Kobayashi, 1921 (?).

This species of fluke, belonging to the family ISOPARORCHIIDÆ, is a common parasite of the air bladder of fishes in India and the Far East, particularly the catfishes and the eels in Japan and Central China Chandler has identified it from the intestine of a human case in Eastern Bengal, where seven specimens of the worm had been expelled after thymol treatment. There is evidence of a second case of human infection with this species from Hunan Province, China. In both instances infection was probably accidental, brought about, no doubt, through the consumption of raw infected fishes. In this respect the infection resembles pharyngeal fascioliasis.

CHAPTER XVI

THE CESTODES OR TAPEWORMS. STRUCTURE AND LIFE HISTORY

STRUCTURE OF THE ADULT CESTODE

THE cestodes or tapeworms are Platyhelminthes which, with the exception of the ciliated embryo of the Order Pseudophyllidea, are parasites during their entire life. Their name, derived from the Greek word κεστός, which literally means "girdle" and has more popularly been translated "tape," indicates that they are elongated ribbon-like organisms. With the exception of a few types (as, for example, *Cylindrotænia*) they are flattened dorso-ventrally. They all possess an antero-posterior polarity. The region usually considered to be the anterior end, technically the *scolex*, and popularly called "the head," is provided with structures for attachment of the worm to the tissues of the host (Fig. 126). It possesses suctorial pockets (*Tænia*, *Dipylidium*), or grooves (*Diphyllobothrium*), and frequently has hooklets. Crusz (1947) has provided microchemical evidence indicating that the hooklets are not chitinous in nature but probably consist of a scleroprotein of the keratin type. The anterior protrusion from the more fleshy part of the scolex, around or on which the hooklets are arranged, is called the *rostellum*. Behind the scolex is the region commonly designated as the "neck."

In the primitive group of cestodes, the **Cestodaria**, the entire region posterior to the "neck" consists of a single unit, but in the more fully evolved species (the **Cestoda**, *sensu stricto*) the segments or *proglottids* are, with few exceptions, multiple (Fig. 127). These proglottids usually originate from the posterior portion of the neck, which is the *region of growth*. Although various degrees of maturity follow one another *ad seriatim* almost imperceptibly, three distinct stages are recognizable in the development of the proglottids. Those immediately behind the region of growth are the *immature proglottids*, *i. e.*, their sexual organs have not yet become differentiated. Behind this first series is one consisting of *mature proglottids*, or those in which the sexual organs are completely formed. Succeeding this series distally is a terminal group of *gravid proglottids*, in which the egg [illegible] ductive organs have more or [illegible] complement of eggs. The entire chain of proglottids, together [illegible] scolex, is called the *strobila*. In its simplest form, the segmented cestode has at any one time only one immature, one mature and one gravid proglottid (*Echinococcus granulosus*, Fig. 174). In most species, however, there are from a few to many proglottids belonging to each stage. The size and number of these proglottids determines the size and length of the tapeworm. Thus, certain species are at most only a few millimeters long, while others may reach many meters in length. When the proglottids become gravid and the eggs are ripe, such segments either break off or disintegrate *in situ*, thus providing that the elongation of the worm does not continue indefinitely.

Tapeworms are covered with a *cuticula*, which is secreted by the underlying *hypodermis* Most investigators agree that the epidermis is lost during the transformation of the oncosphere into a larva. Internal to the hypodermis is a layer of *longitudinal muscles* while the *transverse muscles* constitute the innermost portion of the external girdle of the worm. This is succeeded by a meshwork of *parenchyma cells*, which contain muscle elements but for the most part are undifferentiated and constitute a loose matrix for the internal organs (*i. e.*, nerve cords and fibers, excretory tubules and genitalia).

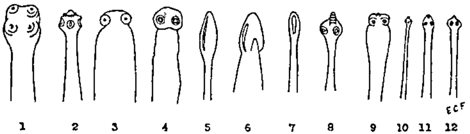


FIG. 126 —Anterior ends of human tapeworms 1, *Tænia saginata;* 2, *T. solium;* 3, *T africana;* 4, *T confusa;* 5, *Diphyllobothrium latum;* 6, *D. cordatum;* 7, *D mansoni;* 8, *Dipylidium caninum;* 9, *Raillietina madagascariensis;* 10, *Hymenolepis nana*, 11, *H diminuta*, 12, *Bertiella studeri*. × 6. (Original)

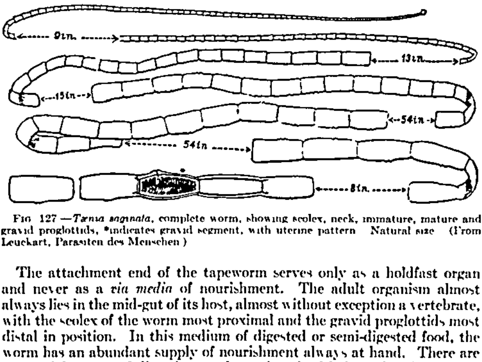


FIG 127 —*Tænia saginata*, complete worm, showing scolex, neck, immature, mature and gravid proglottids, *indicates gravid segment, with uterine pattern Natural size (From Leuckart, Parasiten des Menschen)

The attachment end of the tapeworm serves only as a holdfast organ and never as a *via media* of nourishment. The adult organism almost always lies in the mid-gut of its host, almost without exception a vertebrate, with the scolex of the worm most proximal and the gravid proglottids most distal in position. In this medium of digested or semi-digested food, the worm has an abundant supply of nourishment always at hand. There are no special organs of digestion or absorption, food being taken in through the entire surface of the body and being immediately transformed into parasite tissue or storage products. Thus, growth (*i. e.*, production of new segments) is the immediate result of the absorption of predigested food supplied by the host.

Smyth (1947) has found that tapeworms contain a large amount of carbohydrate, mainly glycogen, which is stored in the parenchyma. There is also a considerable amount of phospholipids but an unusually small amount of proteins, probably in the form of scleroproteins. The integument is freely permeable to water and electrolytes. Immunity to the digestive action of the host's intestinal secretions appears to be due to the character of the integument and not to any anti-enzymes produced by the tapeworm. However, if living eggs, larvae or adults are subject to dilute hydrochloric acid, followed by an alkaline bath and intestinal digestive enzymes, the outermost tissues, as the shell and embryophore of the

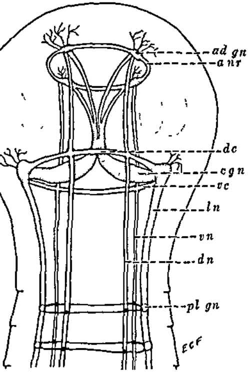


Fig 128 —Schematic diagram of the nervous system of *Moniezia*, a cyclophyllidean tapeworm, showing the nerve trunks, ganglia and commissures in the scolex and first two proglottids *ad gn*, anterodorsal ganglion, *anr*, anterior nerve ring, *cgn*, cephalic ganglion, *dc*, dorsal commissure, *dn*, dorsal longitudinal nerve, *ln*, lateral longitudinal nerve, *pl gn*, posterolateral ganglion, *vc*, ventral commissure, *vn*, ventral longitudinal nerve (Adapted by the author from Tower)

hexacanth embryo within the egg and the bladder of the cysticercus larva, are digested, while the embryo itself and the invaginated scolex of the larva, which do not come in contact with the acid secretions of the stomach, remain unharmed and become activated in contact with bile.

In addition to the basic carbohydrate requirements evidence is accumulating that certain vitamins, pa
the normal development of cestodes
Chandler, 1944, 1946, etc.).

Tapeworms have a very wide range of tolerance to pH, extending from approximately 4 to 11.

Coördination of the entire strobila in the tapeworm's body is imperfect. This is due to the relatively poor development of the nervous system in all

parts of the strobila except in the scolex, where there is a rather complicated set of ganglia and connecting commissures, as well as apical nerves, which are both sensory and motor in function (Fig. 128). Arising from the bilaterally symmetrical "central nervous system" of the scolex (*cgn*) and *proceeding through the complete series of proglottids are the longitudinal* nerve trunks. These usually consist of one main lateral nerve (*ln*) and a

ganglion for each of its six longitudinal nerve trunks and a transverse commissure connecting all of these six ganglia.

The excretory system is primitively like that of the trematodes (*Vide* Figs. 7, 9, 10), with flame-cell termini, capillaries and collecting tubules, the latter emptying into longitudinal trunks. Typically (Fig. 129) each side of the body has both a dorsal and a ventral longitudinal trunk (*dt, vt*) with anterior anastomoses (*aa*) and with a terminal bladder; but in many species, particularly in the adult stage, this has become simplified so that only one pair of lateral trunks is visible, having a transverse anastomosis at the posterior margin of each proglottid. Likewise, since the terminal bladder is lost with the separation of the distalmost segment from the remainder of the worm, the lateral trunks discharge separately from the most distal proglottid still attached to the worm.

The main function of the cestode is egg production. To this end all other functions and structures are subservient. Not only is each worm self-sufficient as far as its sexual products are concerned, but each proglottid is also independent of every other with respect to egg-production. Each

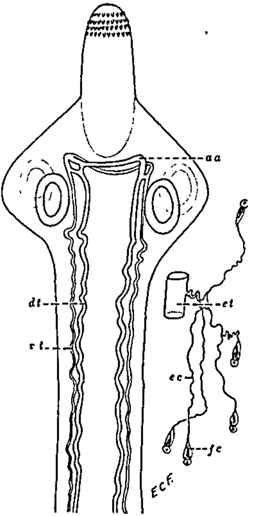
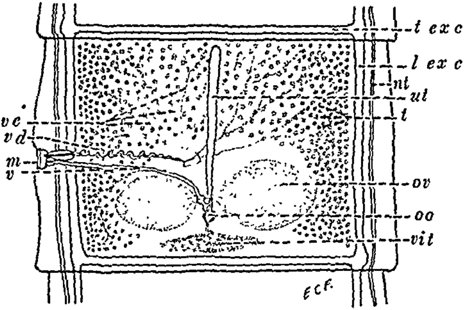


Fig. 129 — Scolex of a very young *Dipylidium caninum* and adjacent "neck" region, showing anterior excretory trunks in a living worm. On the right is a detail of the capillary and flame-cell system opening into a short segment of the dextrodorsal trunk. *aa*, anterior anastomosis, *dt*, dorsal trunk, *ec*, excretory capillary, *et*, excretory trunk, *fc*, flame cell, *vt*, ventral trunk. (Original.)

proglottid contains both male and female reproductive organs. In a few instances (*Dipylidium*, *Diplopylidium*, *Diplogonoporus*) each proglottid is provided with a double set of such organs. While cross-fertilization from one worm to another in close apposition and from one proglottid to another of the same worm is not an infrequent occurrence, it is usual for each proglottid to be self-fertilized.

The *male reproductive organs* consist of both primary and secondary structures (Figs. 130, 131). The follicular *testes* (*t*), which are commonly multiple, are distributed throughout the median plane of each proglottid. *Vasa efferentia* (*ve*) from the testes join one another in dendritic fashion to form the *vas deferens* (*vd*), a coiled or convoluted tubule which proceeds from



... l ex c, lateral excretory
l nerve trunk,
vagina, vd, vas

the middle region of the worm towards the *lateral margin* or *ventrad*, there to open into the *genital atrium* (*m*). In its outermost portion it may become differentiated into *prostate* and *cirral organ*, the two being enclosed in a *cirrus sac* (*cs*) Between the vasa efferentia and the vas deferens there may be a storage reservoir or *seminal vesicle*.

The *female reproductive organs* likewise consist of primary and secondary structures. From the genital atrium a more or less tubular *vagina* (*v*) proceeds towards the *oötype* (*oo*), the latter structure being situated in a median posterior position in each proglottid. The inner end of the vagina is frequently differentiated into a reservoir, or *seminal receptacle* (*sr*), followed by a constricted tubule, the *spermatic duct*. The *ovary* (*ov*) a multiglandular structure, is situated posterior to the mid-plane of the body. Its is connected with the oötype by the *oviduct* (*od*), which receives the ... along its course. The *vitellaria* (*vit*), which may consist

mesenchyma of
into ducts (*vit d*
(*cvd*). Surroun
gland (*Mgl*), the
of the oötype is the *uterus* (*ut*), which may open through a uterine pore (*Diphyllobothrium*) or may end blindly (*Tænia, Dipylidium*). In the former case, the uterus becomes more and more tightly coiled as it elongates to accommodate the eggs which are forced into it from the oötype (Fig. 132, *9, 10, 11, 12*). In the case of species of *Tænia*, the blind pouch develops lateral arms to accommodate the eggs (Fig. 132, *1-4*). In the most immature proglottids *the reproductive organs cannot be discerned. They* become more and more distinct as the proglottid matures, and are most readily studied just as egg-making begins. With the production of a large number of eggs, the need for storage of the ripe sexual products takes

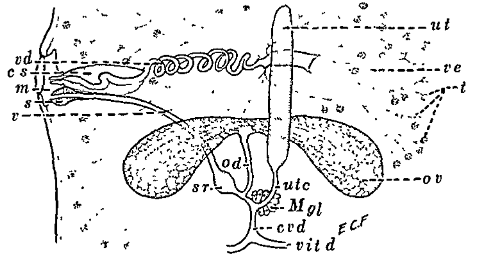


Fig. 131.—Diagram of the genitalia of a cyclophyllidean tapeworm (somewhat schematized) *cs*, cirrus sac; *cvd*, common vitelline duct, *m*, ♂♀ pore or genital atrium, *Mgl*, Mehlis' gland, *od*, oviduct; *ov*, ovary, *s*, sphincter at outer end of vagina, *sr*, seminal receptacle, *t*, testes; *ut*, uterus; *utc*, uterine canal, *v*, vagina; *vd*, vas deferens, *ve*, vas efferens, *vit d*, vitelline duct (Original)

precedence over egg production and the sexual organs, at least in the higher groups of the cestodes (the **Cyclophyllidea**), all gradually atrophy, with the exception of the uterus, which becomes greatly distended and tends to fill the entire proglottid. The shape of the gravid uterus (Fig. 132, *1-12*) is frequently of diagnostic value in determining the species of tapeworm.

The egg is assembled in the oötype. It consists of the fertilized ovarian cell and an aggregation of "yolk cells," the whole being surrounded by an egg-shell. In the **Pseudophyllidea** (*i. e.*, *Diphyllobothrium*, Fig. 136, *Diplogonoporus*, Fig. 145), which possess a uterine pore, the egg is ovoidal in contour like that of a trematode, and is provided with an operculum. In
... the **Cyclophyllidea** (*i. e., Tænia,*
...*menolepis*, Figs. 155 *C*, 157 *C*),
...g cell is frequently surround-

ed not only by an egg-shell but also by additional embryonic membranes. In most species these outer membranes surround each egg individually; in the case of *Dipylidium* (Fig. 153 *C*) one uterine or embryonic membrane envelops a group of several eggs. In the **Pseudophyllidea** the eggs are operculate and escape from the uterus while they are still immature. Development is completed and hatching occurs in water. In the **Cyclophyllidea** the eggs are not operculate and are mature when set free from the uterus.

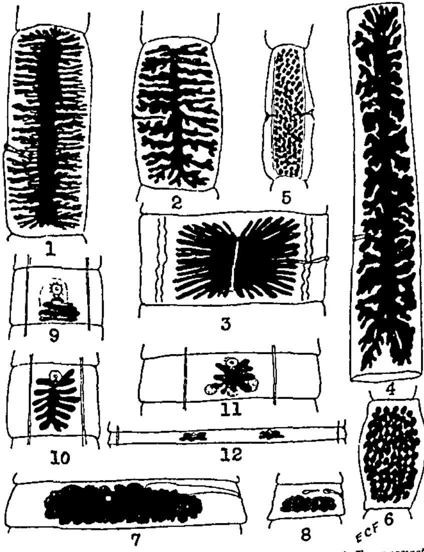


FIG 132 —Gravid proglottids of the important human tapeworms 1, *Taenia saginata*; 2, *T* ... 6. *Raillietina madagascariensis*, ... 10, *D cordatum*; 11, *D* ... 5. (Compiled and adapted from various sources)

... worms. ... s

The ... g viscous medium, where their existence is dependent on their ... Here they must ... an equilibrium against peristaltic and food movements. As previously stated, they are ... obtain adequate oxygen and nourishment.

known to have a high glycogen-fat content as compared with proteins. Some investigators regard this glycogen reserve as a source for oxygen. Tapeworms also have a high reserve of calcium carbonate, which may serve *as a buffer for the body tissues against hyperacidity. Wardle (1935) has* compared the adult tapeworm within its host to "a swimmer breasting a strong current and barely able to maintain his position against the current." Thus, under conditions of starvation, intoxication, or increased peristalsis, the equilibrium is frequently not maintained, the greater portion of the worm is separated from the scolex, and passes down and out of the bowel. Anthelmintic medication utilizes this information by anesthetizing the worm, while stimulation of the peristaltic movements of the bowel wall by purgation hastens the evacuation of the parasite.

Jones (1945) has studied cell division in 15 species belonging to two families of cyclophyllidean tapeworms, the Hymenolepididæ and the Dilepididæ, and has demonstrated that mitosis and meiosis occur as they do in the greater majority of animal species. He distinctly rejects the assumption of Child (1904), based on studies of *Moniezia expansa*, that amitosis occurs as a normal process

THE LIFE CYCLE OF CESTODES

In the **Cyclophyllidea** the embryo is already fully developed and ready to hatch upon its escape from the uterus of the parent worm. In the case of the **Pseudophyllidea** the eggs are discharged, while still immature, through the uterine pore. In cyclophyllidean species escape is frequently effected through rupture of the uterus The embryo within the egg is designated as the *oncosphere* (ὄγκος, hook, σφαῖρα, ball), or, because of the fact that it usually possesses three pairs of hooklets, is called the *hexacanth* ἕξ, six, ἄκανθα, spine) embryo Reid (1946) has observed a pair of unicellular penetration glands, opening through pores at the anterior end of the embryo, secreting a substan [illegible] entrance into the tissues of [illegible] shell layers is an enveloping [illegible] ately surrounds the oncosphere The oncosphere, together with its embryophore is referred to as the *coracidium*. In the **Pseudophyllidea**, with few exceptions, the mature embryo is provided with a ciliated embryophore. The egg hatches in a moist medium and the emergent organism swims about in the water. Practically all other cestode embryos are non-ciliated, and hatch only after being ingested by their intermediate host. Venard (1938) favors the view that the stage of cestodes hatched from the egg is a "larva" rather than an "embryo."

With the exception of *Hymenolepis nana*, all of the known human tapeworms require two or more hosts, a *definitive host* for the mature stage of the worm, and one or more *intermediate hosts* for the larval stage or stages. In [illegible] mouse) serves [illegible] experimental [illegible] *olaenia noei*, a [illegible] The tadpole stage of the frog serves as the host for the cysticercoid larva, while canni-

possibly capable of producing both an intestinal and a somatic infection in man. In the former case, man is the definitive host; in the latter case, the intermediate host. Man is the only known definitive host of *Tænia saginata*. In *Hymenolepis nana* infections man serves both as intermediate and definitive host.

While the eggs (oncospheres) of tapeworms reach the first intermediate host through feeding on more or less diluted fecal wastes, infection of the definitive host (or, in the case of *Diphyllobothrium*, the second intermediate host) is brought about from the ingestion of the infected first intermediate host or part of its tissue. Thus, the fish or the frog acquires somatic sparganosis through consumption of the *Cyclops*, which is the first intermediate host of the worm. Man, dogs and cats acquire the intestinal infection from consumption of the raw, infected second intermediate host. *Dipylidium* and *Hymenolepis diminuta* infections in man or other mammals result from the accidental ingestion of the arthropods respectively involved as intermediate hosts. The presence of *Tænia solium* and *Tænia saginata* in man is due to eating raw flesh of "measly" pork or beef. *Hymenolepis nana* and *Echinococcus* infections in man are due to unclean habits of the infected individual. The time required for the maturing of the adult tapeworm in the human intestine varies from a few days to several weeks, depending on the species of worm.

CHAPTER XVII

THE CESTODES OR TAPEWORMS. CLASSIFICATION

THE BASIS OF CLASSIFICATION

ALTHOUGH the system of classification developed by Monticelli (1892) was employed by many distinguished workers during the next quarter century, it contains certain inconsistencies, due to the grouping within the same subclass of organisms which superficially resemble one another but are fundamentally different. Thus, Monticelli placed *Archigetes* and *Caryophyllæus* with *Amphilina* and *Gyrocotyle* in the subclass **Cestodaria**. Fuhrmann (1931) has rectified this inconsistency and has provided a system essentially sounder than his predecessors. The classification presented in this manual is an adaptation from Fuhrmann.

CLASS CESTOIDEA (RUDOLPHI, 1808) FUHRMANN, 1931

[illegible] alimentary canal; body in almost all species divided into proglottids.

Subclass I. Cestodaria Monticelli, 1892, emend. Fuhrmann, 1931

Body not divided into proglottids; only a single set of reproductive organs. Oncosphere contains 10 to 12 (*i. e.*, 5 to 6 pairs of) hooklets. No human representative. Example: *Amphilina foliacea* (Rudolphi, 1819).

Subclass II. Cestoda (van Beneden, 1849) Monticelli, 1892, emend. Fuhrmann, 1931

Body typically with scolex and series of proglottids, each containing one set (rarely two sets) of male and female reproductive organs. Oncosphere typically contains 6 (*i. e.*, 3 pairs of) hooklets.

ORDER I. PSEUDOPHYLLIDEA CARUS, 1863

Scolex typically unarmed, with two opposite sucking organs (the *bothria*) which may become fimbriated or tubular, or may be partially or wholly suppressed; never with four suckers or accessory proboscides; usually multisegmented, rarely like the Cestodaria containing a single set of reproductive organs (*viz.*, in family Caryophyllaeidæ). All species parasitic in man are found in the Family Diphyllobothriidæ Lühe, 1910.

Family DIPHYLLOBOTHRIIDÆ Lühe, 1910

Scolex unarmed, of a variety of patterns, usually serving as tubular adhesive organ. Openings of cirrus and vagina mid-ventral and anterior to the patent uterine pore. Eggs operculate, with a single, relatively thick shell; mature embryo (oncosphere) ciliated; procercoid and plerocercoid larval stages in one or more intermediate hosts. Adults in intestinal tract of

vertebrate hosts, most frequently birds and mammals. Human representatives: [illegible] *D. cordatum* (Leuckart, 1863); *D. ho*[illegible] 1929; *Diplogonoporus grandis* (Blanchard, 1894); *Digramma brauni* (Léon, 1907); *Ligula intestinalis* (Goeze, 1782); larval forms, *Sparganum mansoni* (Cobbold, 1882); *Sparganum proliferum* (Ijima, 1905); *S. baxteri* Sambon, 1907, and probably other related species.

The single specimen of the species *Diancyrobothrium taenioides* Bacigalupo, 1945, for which a family Diancyrobothriidæ was specially erected, is probably an abnormal or atypical representative of *Diphyllobothrium latum.*

ORDER II. TRYPANORHYNCHA DIESING, 1863

Scolex with two or four sucking grooves and also at apex four protrusile proboscides armed with many hooks. Genitalia as in the Tetraphyllidea, except that the vitellaria are more abundantly developed; uterine pore completely or apparently patent, or closed. Complete life cycle unknown, larval stages in fishes and marine invertebrates, rarely in reptiles. No human representatives; adults in spiral valves of selachians, rarely in ganoids. Example: *Tetrarhynchus bisulcatum* (Linton, 1889) Linton, 1897.

ORDER III. TETRAPHYLLIDEA (CARUS, 1863) BRAUN, 1900

Scolex with four, very flexible sucking cups of variable shapes and patterns; male and female sex pores always lateral. Oncospheres developed *in utero.* Two or one intermediate hosts required; vitellaria with numerous follicles. No human representative; adults in alimentary canal of fishes, amphibians and reptiles. Example: *Thysanocephalum crispum* Linton, 1889.

ORDER IV. DIPHYLLIDEA (VAN BENEDEN, 1848) BRAUN, 1900

Scolex consisting of head and shaft; two bothria, each dorsal and ventral on the head, appearing fused medially; rostellum provided with dorsal and ventral hooks; neck short; proglottids frequently become separated from strobila before maturity. Genitalia as in the Tetraphyllidea, except that the sexual pores open ventrally. Larval stages in Crustacea and Mollusca. No human representative; adult worms in intestine of selachian fishes. Example: *Echinobothrium affine* Diesing, 1863.

ORDER V. CYCLOPHYLLIDEA BRAUN, 1900

Scolex with four depressed cup- or saucer-shaped suckers, and in the center usually an apical organ or rostellum of varied form, frequently armed with hooks; vitellaria a single mass characteristically posterior to the ovary, sex pores, when patent, usually open laterally. All species parasitic in man are found in the

SUPERFAMILY TÆNIOIDEA ZWICKE, 1841

Body almost always flattened; suckers four, simple; egg shell without operculum, with one or more layers; embryo (oncosphere) typically mature on disintegration of gravid proglottid, not ciliated, larvæ in invertebrates or vertebrates, adults in intestine of vertebrates.

Family ANOPLOCEPHALIDÆ Cholodkowsky, 1902

Scolex unarmed, without rostellum; suckers large, unarmed; neck region lacking. Human representative: *Bertiella studeri* (Blanchard, 1891).

Family MESOCESTOIDIDÆ Furhmann, 1907

Members of this family are unique among cyclophyllidean tapeworms in having the genital atrium mid-dorsal in position rather than lateral, in possessing two entirely separate vitelline glands and, in addition, in having the eggs in gravid proglottids concentrated in a single mass enclosed in a fibrous capsule. Human representative: *Mesocestoides variabilis* Mueller, 1928.

Family DILEPIDIDÆ Fuhrmann, 1907, emend. Lincicome, 1939

Rostellum, if present, armed; suckers unarmed or rarely armed; uterus broken up into egg-capsules; genital organs single or occasionally double. Human representative: *Dipylidium caninum* (Linn., 1758).

Family DAVAINEIDÆ Fuhrmann, 1907

Rostellum cushion-shaped, armed with numerous hammer-shaped hooks in two rows, suckers armed; uterus broken up into egg capsules. Human representatives: *Raillietina madagascariensis* (Davaine, 1869); *R. celebensis* (Janicki, 1902), *Raillietina asiatica* (v. Linstow, 1901); *R. demerariensis* (Daniels, 1895).

Family HYMENOLEPIDIDÆ Fuhrmann, 1907

Proglottids usually broader than long; testes one, two, or more often three, rarely more (twelve); genital pores unilateral; uterus persistent, sac-like. Human representatives: *Hymenolepis diminuta* (Rud., 1819); *H. nana* (v. Siebold, 1852); *Drepanidotænia lanceolata* (Block, 1782).

Family TÆNIIDÆ Ludwig, 1886

Scolex armed or unarmed; uterus with median longitudinal stem and lateral branches; genital pores irregularly alternating. Human representatives: *Tænia solium* Linn., 1758; *T. saginata* (Goeze, 1782); *T. confusa* Ward, 1896; *T. africana* v. Linstow, 1900, *T. tæniæformis* (Batsch, 1786); *Multiceps multiceps* (Leske, 1780); *M. glomeratus* Railliet and Henry, 1915; *M. serialis* (Gervais, 1845); *Echinococcus granulosus* (Batsch, 1786).

CHAPTER XVIII

THE PSEUDOPHYLLIDEAN CESTODES

ORDER PSEUDOPHYLLIDEA CARUS, 1863

THE cestodes belonging to the Order **Pseudophyllidea** are characterized by having a spoon-like or spatula-like scolex, with simple, median longitudinal channels on opposite surfaces, the dorsal and ventral sides, to form the bothria, or suctorial grooves. The uterus is provided with a pore, the eggs are operculate, with a single shell layer, and the oncosphere is ciliated. The species occurring in man are restricted to the family **Diphyllobothriidæ** Lühe, 1910, in which the rosette-shaped or coiled uterus, as well as the vagina and cirral organ, open ventrad, and the vitellaria are lateral in position.

Considerable confusion exists as to the number of valid species of the genus *Diphyllobothrium* in mammalian hosts, and some workers even question the validity of employing this generic name for the species reported from land mammals (Wardle, McLeod and Stewart, 1947). This point can be settled only by a careful morphological study of the adult worms in conjunction with life history investigations.

GENUS DIPHYLLOBOTHRIUM COBBOLD, 1858

(genus from δις, twice, φύλλον, leaf, and βόθρος, groove or sucker)

A. Subgenus DIPHYLLOBOTHRIUM (with a "Rosetted" Uterus)

Diphyllobothrium latum (Linnæus, 1758) Lühe, 1910. (The fish tapeworm of man, causing diphyllobothriasis or fish tapeworm infection.)

Synonyms.—*Tænia lata* Linn., 1758; *Tænia vulgaris* Linn., 1758; *Tænia membranacea* Pallas, 1781, *Tænia tenella* Pallas, 1781; *Tænia dentata* Batsch, 1786; *Tænia grisea* Pallas, 1796; *Bothriocephalus latus* (Linn., 1758) Bremser, 1819, *Dibothrium latum* (Linn , 1758) Diesing, 1830; *Bothriocephalus balticus* Kuchenmeister, 1855; *Bothriocephalus cristatus* Davaine, 1874; *Bothriocephalus latissimus* Bugn , 1886; *Dibothriocephalus latus* (Linn., 1758) Luhe, 1899, *Bothriocephalus tænioides* Léon, 1916, *Dibothriocephalus minor* Cholodkowsky, 1916

Historical and Geographical Data.—*Diphyllobothrium latum*, the "broad fish … recognized as a species of tape-

…erred to in

…it requires

…orphologic-

of fishes, while its adult stage is never found in fishes but in …

The adult worm, *Diphyllobothrium latum*, has long been known as a common human parasite in Northern Italy (around lakes Como, Maggiore and Varese), Switzerland, parts of Germany, and in the Baltic countries, including East Prussia, Poland, Lithuania, Latvia, Estonia, Finland, Sweden, Denmark and European Russia In Ireland this parasite has been known since 1844 (Harris, 1945) In western Russia 2 to 100 per cent of the human population is parasitized by this

tapeworm, and practically all food fishes are heavily infected. Within more recent times it has been found to be a common parasite of man in Roumania and the Danube delta, in the vicinity of Lake Tiberias in Palestine, Turkestan, extensive areas in Siberia, Northern Manchuria and Japan Its presence has apparently been authenticated for the Philippines (1935) It is established in several foci in North

eastern Canada," where it is also found in silver foxes, cats and bears. Although its focal center in Canada is Manitoba, it extends from the Gulf of the St. Lawrence to the coast of British Columbia The Arctic species of fish tapeworm in North America is believed to be different from *D. latum*. Summers and Weinstein (1943) and more recently Hood (1947) have demonstrated that there is a small isolated focus of the infection in northern Florida, where Negro children and dogs have acquired the disease from locally caught fish. Records of its presence outside of the northern temperate zone require verification. Magath (1937) suggests that reports of cases from the Great Lakes district of Uganda, from Bechuanaland, Angola and Madagascar are not conclusive. Similar scepticism may be justified regarding reports from Papua, New Guinea, and from Nigeria, yet autochthonous diphyllobothriasis

domestic dog, *Dusicyon gymnocercus gymnocercus*, *Urocyon cinareoargentatus*, and *Canis lupus occidentalis;* from the domestic cat, *Felis concolor*, *F. mellivora*, *F. hernandesii*, *F. macroura*, *F. pardus*, *F. leo* and *F. mitis;* from the mongoose (*Herpestes leucurus*), the walrus (*Odobænus rosmarus*), seals and sea-lions (*Leptonyx*

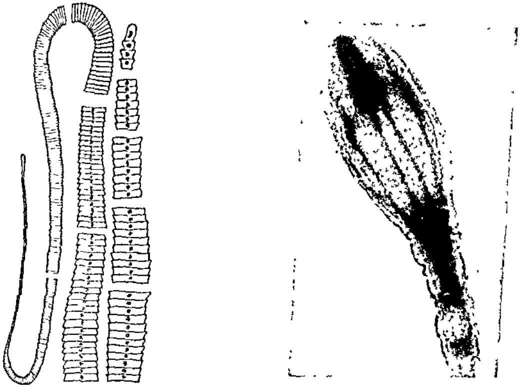
Structure of the Adult Worm.—When freshly expelled from the human intestine, the worm (Fig. 134 *A*) is ivory colored but it may become grayish on fixation Young mature specimens from the human host may measure only 3 meters in length but older specimens may attain a length of 10 meters or more, with a total of 3000 or more segments. The scolex (Fig. 134 *B*) is small, spatula-shaped, with rather deeply sulcated dorsal and ventral grooves It measures about 1 mm. in cross-section by 2.5 mm. in length.

to take place as a result of transverse constriction of undifferentiated proglottids along the entire proximal portion of the strobila (Fuhrmann, 1931; Wardle, 1935). As the organism is followed farther and farther distad, these immature proglottids become more and more fully developed, until they are recognized as mature proglottids (Fig. 135). With the process of egg production initiated, the mature proglottids become transformed into gravid proglottids, *i. e.*, those in which the uterus has become elongated and twisted back and forth upon itself in the characteristic "rosette" pattern to accommodate the eggs (Fig. 132, *H*). Mature and gravid proglottids together occupy about four-fifths of the length of the worm.

The typical mature proglottid of *Diphyllobothrium latum* (Fig. 135), as is found in the middle third of the worm, is provided with both primary

and secondary male and female reproductive organs. T[illegible]

[illegible] efferentia converging at various levels to unite [illegible] efferens, the several vasa the latter originating in the mid-plane at the beginning of the posterior third of the body and proceeding anteriad as a very highly convoluted tubule, enlarging at its outer terminus to form a seminal vesicle and ending in a muscular cirral organ, which opens on the anterior aspect of the common genital pore.



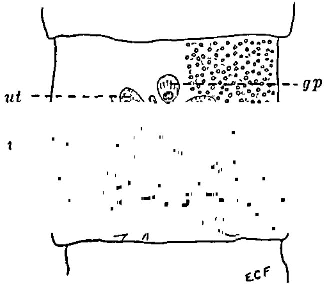
A B

FIG 134.—*A*, Strobila of *Diphyllobothrium latum*, two-thirds natural size (partly after Leuckart). *B*, head of *D. latum*, lateral view, × 35. (From Magath)

The ovary is a symmetrically bilobed structure, situated on the ventral surface in the posterior third of the segment. Between its two lobes is the Mehlis-gland or "shell-gland" complex. From the common male and female genital pore there arises a narrow tubule, the vagina, which proceeds directly posteriad, coiling somewhat at its enlarged inner end to form the seminal receptacle. In the lateral fields ventral to the testes there are vitelline glands, the ducts of which converge to form right and left vitelline ducts, which, in turn, fuse into a common vitelline duct. The inner end of the vagina, together with the common vitelline duct, joins the oviduct to enter the oötype on the median anterior face of Mehlis' gland From the left anterior angle of the oötype there arises the uterus, which twists back and forth from side to side, and finally terminates in a uterine or birth pore in the mid-ventral line, a short distance behind the common genital pore. The amount of twisting of the uterus, *i. e.*, the "rosetting" of the

uterus, depends on the number of eggs which it has been required to accommodate.

Spermatozoa produced in the multiple testes reach the vas deferens *via* the vasa efferentia and are temporarily stored in the seminal vesicle. They escape from the male system through the common genital atrium and are ordinarily transferred directly into the vagina, although the presence of a muscular cirral organ indicates that cross-insemination is possible. Once within the vagina, [illegible] ed in the seminal receptacle. [illegible] rmation of the egg, consisti [illegible] follicles from the vitellaria, spermatozoa, and shell-gland material, are all assembled in the oötype as they are required, and the completed egg is then pushed out into the proximal region of the uterus. The eggs in the inner portion of the uterus are necessarily less mature than those in the outer coils. In size the former are somewhat smaller and in color more hyaline.



[illegible]

As the uterus becomes more and more distended with eggs, the sphincter guarding the birth pore becomes intermittently relaxed, so that in gravid [illegible] ating [illegible] s the [illegible] d decrease in egg-laying until it ceases entirely. Unlike the cyclophyllidean cestodes, the terminal gravid proglottids of pseudophyllidean species are never normally separated from the parent stem, but as they cease to function the distalmost proglottids gradually disintegrate and are finally sloughed off. In this way it is estimated that a single worm may discharge as many as a million eggs *per diem*.

The metabolic processes in *D. latum* have been studied by Friedheim (1933), Wardle (1935) and other investigators.

The Life Cycle.—The eggs of *Diphyllobothrium latum* and related species, when discharged from the par[illegible]
are provided with abundant [illegible]
it develops. In the case of *D* [illegible]
They are usually yellow to golden-brown in color, and have an *operculum* at one end which becomes more conspicuous as the time for hatching approaches. They average 70 μ in length by 45 μ in breadth. In man, and the bear in Canada, a high percentage of the eggs evacuated in the feces is fertile but most of those in dog's feces are sterile (Cameron, 1945). These eggs are quite resistant to chemicals but rapidly become non-viable under conditions of desiccation or putrefaction. The period for development, which occurs in water (*i. e.*, in diluted feces), varies from eleven to fifteen days at 15 to 25° C. temperature of the water. Upon maturing, the oncosphere, covered with its ciliated *embryophore*, escapes through the opercular opening in the shell, casts off its embryonic envelope, and swims about in the water (Fig. 137). Within about twelve hours the embryo must be ingested by a suitable crustacean host, or perish, since it is incapable of feeding. The demonstrated hosts include the following copepods: *Diaptomus vulgaris*, *D. gracilis*, *D. graciloides* and, to a lesser extent, *Cyclops strenuus* Fischer (Fig. 138) and *C. vicinus* Uljanin in Europe; and *D. oregonensis*, *D. sicilis* and *D. siciloides* in North America.

From the intestinal canal the embryo migrates into the hemal cavity of this first intermediate host, becoming transformed in the course of two or three weeks into an elongated oval object, the *procercoid larva*, which measures in length from 50 to 60 μ, while immature, up to 550 μ, when mature, and still possesses the three pairs of hooklets on its caudal appendage (*cercomer*) (Fig. 139*A*). Usually only one or two such larvæ develop in a single crustacean.

If the infected crustacean is now ingested by a plankton-feeding fresh-water fish, the larva is set free in the fish's stomach, and in the course of three or four days penetrates its wall and wanders through the body cavity into the flesh and connective tissue, where it becomes transformed into a *sparganum*, or plerocercoid larva, measuring up to 6 mm. or more in length, and lying free between the muscle fibers rather than in an adventitious sheath or capsule. According to the investigations of Fuhrmann these larvæ within the second intermediate host multiply several fold by asexual methods, but Vergeer (1937) is opposed to this view and suggests that after several months in the fish flesh they die. The sparganum (Fig. 139, *B*, *C*) is glistening, opaque white, has an antero-posterior polarity, has an invaginated anterior end which may serve as an attachment organ, and, on contraction, may appear to have a more or less pronounced pseudo-segmentation. Various fresh-water fishes, particularly those of lakes and mountain streams, serve as second intermediate hosts of the infection. The larger, edible fishes probably do not acquire their infection directly from the infected copepods, but indirectly from eating smaller fishes which have become infected Among the food fishes, which are probably the most common sources of human infection, the following species have been incrimin-

ated: the European pike (*Esox lucius lucius*), the European perch (*Perca*

gorbuscha), the dog salmon (*O. keta*), the sockeye or blueback salmon (*O. nerka*), *Hucho perryi* and the rainbow trout (*S. irideus*) from Japan; the European barbel (*Barbus vulgaris*) from Lake N'gami in Africa (?); and from northern North America the barred pike, *Esox lucius estor*, the wall-eyed or blue pike (*Stizostedion vitreum*), the sand-pike or sauger (*S. canadense griseum*), and the American burbot (*Lota maculosa*). These and other fresh-water fishes frequently harbor in their flesh other, related, species of

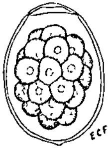


FIG 136.—Egg of *Diphyllobothrium latum*. × 500 (Original.)

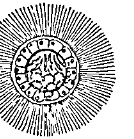


FIG 137.—Free-swimming hexacanth embryo of *D. latum* × 500 (After Rosen.)

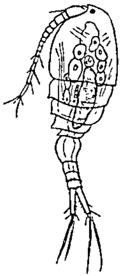


FIG 138.—*Cyclops strenuus*, containing procercoid of *Diphyllobothrium latum*. (After Rosen.)

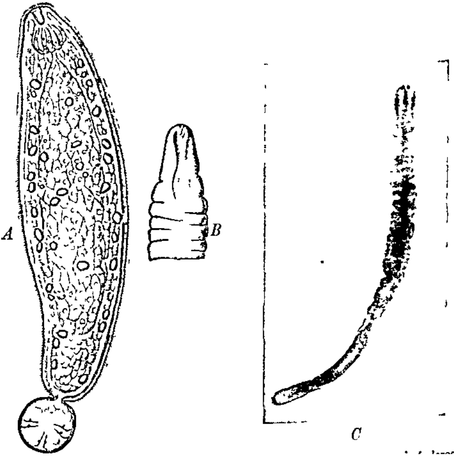
spargana, which must not be mistaken for those of *Diphyllobothrium latum*. Thus, records of
of human infecti
accompanied by
the spargana is
criminated.

In man the worms may remain active for several years, or they may be discharged spontaneously. At times they probably disintegrate and die slowly within the bowel, without objective evidence. In heavily endemic areas, as in parts of the Baltic countries and Siberia, multiple infection is common, and hundreds of feet of strobilæ may be evacuated from a patient following specific therapeusis.

Cameron (1945) suggests that *D. latum* of Canada may not be identical with this parasite in Europe and Asia but may be an indigenous parasite of the brown bear.

Epidemiology.—The wide distribution of these piscine hosts in North America makes the possible dispersal of this parasite a serious public health menace. On consuming insufficiently cooked flesh and possibly the roe (caviar) of infected fish, man is exposed to the infection, the worm proceeding to develop within his intestinal tract and maturing in five or six weeks after exposure, at the end of which time eggs first appear in the feces.

In Finland *D. latum* infection is today, as in previous decades, an important clinical and public health problem. About fourteen per cent of the population, or 600,000, harbor the parasite.



...cercoid

In the endemic foci in North America, the Scandinavian and Jewish ... infected In Winnipeg (Manitoba) in ...

... and even into Kentucky, are known to have been the ... fection in those extra-endemic localities.

Pathogenesis, Pathology and Symptomatology.—The presence of *Diphyllobothrium latum* in the human intestine at times is associated with the clinical picture commonly known as "bothriocephalus-anemia." The patient, who gives a past history of having eaten uncooked or rare fish, first experiences a condition of malaise and possibly of jaundice. On physical examination there is a noticeable anemia, and possibly slight hemorrhage of the oral mucosa. There may be slight edema of the face and joints. Following experimental self-infection, Tarassov (1937) experienced marked abdominal pain, lost 8 kilograms in weight, and became so weak he required hospitalization.

In an inquiry on the relationship between fish tapeworm infection and pernicious anemia in Finland, von Bonsdorff cites Tötterman's figures (1944) that on the average the anemia occurs in about 0.3 to 1.0 per cent of persons harboring the worm. However, in individuals with a history of vomiting the worm anemia is significantly much higher. By means of an *intestinal tube, as well as by study of operative reports on tapeworm* patients, data were accumulated to indicate that the worm is usually attached to the wall of the ileum, less commonly of the colon, and in these patients there is rarely an associated anemia; but at times the worms are present at the jejunal level, once were found operatively in the gall bladder, and in such patients there is positive correlation with pernicious anemia. The investigator believes that when the worm resides at the more proximal level its metabolites inhibit the combining of the extrinsic and intrinsic factors of Castle, with resultant disease. A remission of the anemia may occur without loss of the worm This is interpreted by von Bonsdorff as resulting from migration of the tapeworm to a more distal position in the intestine. When the food supply of the population is inadequate, as occurred in 1942 in Finland, pernicious anemia in tapeworm patients was two to three times as common as in 1943 when there was sufficient protein available (Totterman).

Masses of *D. latum* in the small intestine may produce acute obstruction and may cause symptoms suggesting cholecystitis or peptic ulcer.

Blood examination occasionally shows an erythropenia (500,000 to 2,000,000), with nucleated red cells, anisocytosis and poikilocytosis; a reduction in the white cells, at times with a more or less pronounced eosinophilia. The hemoglobin percentage may be as low as 25 or 30, although the color in dex may be above unity. There is frequently a slight irregular elevation of temperature. Some clinicians believe that the symptoms are due to the absorption of by-products from the degenerating dead proglottids of the worms, while others favor the view that the living worm secretes a substance toxic to the host. In the majority of cases, however, there are no clinical symptoms.

In an analysis of the literature on "bothriocephalus-anemia," Birkeland (1932) found that the actual number of cases of anemia is indeed small compared with the percentage of persons infected with *D. latum*. More than 70 per cent of all recorded cases of the anemia have occurred in Finland, where the population appears to have a predisposition to pernicious anemia. While infection with the tapeworm may be a precipitating factor of the syndrome, by providing for, or allowing, toxic products to be absorbed from

the intestine, there is no convincing proof that the worm is the primary cause of the disease. Totterman (1945) found fourteen per cent incidence of anemia among patients harboring *D. latum* in Finland. He recognized two types of anemia among these individuals, (1) a pernicious type amenable to treatment with Castle's extrinsic factor present in yeast or liver, and (2) a hyperchromic type not responsive to Castle's factor but improved following removal of the worms.

Wardle and Green (1941) have demonstrated in experimental *D. latum* infections in man and dogs a gradually developing hyperchromic anemia, with a tendency towards macrocytosis. This apparently results from the absorption of unsaturated fatty acid liberated by the tapeworm, thus confirming the hypothesis of Faust and Tallqvist (1907).

Diagnosis.—Based on the recovery of the characteristic eggs (Fig. 136) from the feces of the patient, and occasionally of evacuated proglottids.

Neither in the copepod host (procercoid stage) nor in infected fish (sparganum larva) can *D. latum* be distinguished from other species of *Diphyllobothrium* which are natural parasites of birds (Thomas, 1947).

Therapeusis.—The two most efficient anthelmintics, utilized for the re- [illegible] from the intestinal [illegible] These drugs [illegible]

(1) *The Oleoresin of Aspidium (Dryopteris filix-mas).*—The patient eats only soups, milk and toast the day before treatment and before retiring takes 2 tablespoonfuls of Glauber salts (sodium sulfate) dissolved in a glass of water. On the morning of treatment breakfast is omitted (plain tea or black coffee excepted) and the patient remains in bed. The drug is administered in gelatin capsules in 3 equal doses at 7, 7:30 and 8 A. M. Each divided dose consists of 0.6 to 1.2 grams (10 to 20 minims) for an adult, 1 minim for each year of age for a child. At 10 A. M. follow with a Glauber salts purge. No food is allowed until a copious bowel movement has been obtained. All stools up to forty-eight hours should be carefully examined for the head of the worm. [illegible] repeated in [illegible] freshness of the drug, the careful coöperation of the patient and the pre- and post-treatment purgation.

Some physicians prefer to administer the drug, together with the purgative, through a duodenal sound. The therapeutic is made up in an emulsion as follows:

Oleoresina aspidii, 4 cc.
Mucilage of acacia, 60 cc.
Sat. sol. sodium sulfate, 60 cc.

Preparation of the patient is similar to that for the orthodox treatment The emulsion is intubated all at one time. No post-treatment purgation is needed, since the purgative agent is incorporated in the emulsion.

The extract of *Aspidium* is probably purer than the oleoresin, but is usually less potent [illegible] of 3 cc., [illegible] in two [illegible] preceded the night before by Glauber salts purgation and [illegible]

hours by saline purgation. In severe cases, extreme care should be taken to prevent absorption of the drug into the system. The drug is contraindicated in patients suffering from gastro-enteritis, nephritis, pregnancy, elevated temperature, hepatic dysfunction and low serum calcium in the blood. A serious disadvantage of this drug is the likelihood that it may digest the head and neck of the worm, so that the stools passed following treatment will not necessarily provide evidence that the parasite has been eradicated.

It is probable that in some instances *D. latum* can be eradicated by administration of atabrine, as advocated by Neghme and Faiguenbaum (1947) for the treatment of taeniasis; or by transduodenal intubation of an emulsion of hexylresorcinol, as tested by Brown (1948) and by Hernández-Morales and Santiago-Stevenson (1949) for taeniasis. (Vide p. 306.)

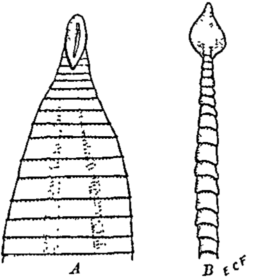


Fig. 140.—*Head of Diphyllobothrium cordatum*, from dog. *A*, dorsal view, *B*, lateral view. × 12 (Original.)

Prognosis.—Good, provided the worms are completely removed. The symptoms usually clear up following evacuation of the worms, the blood picture returns to normal, and the patient proceeds to an uneventful recovery. At times liver and iron are indicated as supplementary therapeutics.

Control.—Thorough cooking of all fish in suspected areas is indicated. Public health officials in non-endemic areas should erect barriers to prevent its introduction from endemic foci. Fish should not be shipped out of endemic areas unless previously subjected to freezing temperatures (*viz.,* -10° *C.) for at least twenty-four hours (Kajava, 1913; Magath and Essex, 1931).* Sewage from infected cities should be adequately filtered or sterilized with formaldehyde or chlorine before being discharged into rivers and lakes. Summer fishing for pike and other fish hosts of the sparganum should be prohibited in endemic areas, since this is the season of maximum fish infection. *Barriers should be erected to prevent the shipment of potentially* infected fish out of endemic areas unless previously frozen long enough to guarantee sterilization. Housewives and others who taste fresh-water fish before it is cooked should be warned of the danger of such practice.

Dogs do not appear to be important as reservoirs of infection, since the eggs of *Diphyllobothrium latum* discharged in their feces are only about 5 per cent viable.

Diphyllobothrium cordatum (R. Leuckart, 1863). (The cordate tapeworm.)

Synonyms.—*Bothriocephalus cordatus* R. Leuckart, 1863; *Dibothriocephalus cordatus* (R Leuckart, 1863)

Biological Data.—*Diphyllobothrium cordatum*, a common parasite of the seal, the

tinguishing characteristics (Fig. 140) are the compressed cordate scolex, with suctorial grooves on the dorsal and ventral surfaces, the almost complete absence of a neck, and the t

of six to eight coil

75 μ in length by

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st.

Pathogenicity and Symptomatology.—Unknown.

Diagnosis.—On the basis of finding *Diphyllobothrium* eggs in the stool of a suspected patient, administering a specific anthelmintic, and identifying the recovered worm by its specific characters. According to Scott (1935), adults are distinguished with difficulty from *D. latum* and *D. cordiceps* (Leidy, 1872).

Therapeusis.—Unstudied, but oleoresin of *Aspidium* is probably specific.

Prophylaxis.—Abstinence from eating raw fish.

Diphyllobothrium parvum (Stephens, 1908) Faust, 1929.

Synonym.—*Dibothriocephalus parvus* Stephens, 1908

This tapeworm, which was found once by Elkington in a Syrian who had recently immigrated to Tasmania, was described as a new species on the basis of its smaller size and different egg measurement (av 59 2 by 40.7 μ) from *D latum* The scolex was not recovered Some helminthologists believe it to be a dwarfed *D latum* and this is quite possible. A second case harboring this worm has been reported by Léon (1915) from Roumania Yoshida (1924) has described a third specimen from Japan Stiles and Hassall (1926) also record this species from Persia and from Minnesota (U. S. A.). In none of these cases has the head been obtained. Magath (1929) has produced the entire strobila in experimentally infected dogs in Minnesota, and feels that the worm is an undersized *D. latum.*

stitute atypical or abnormal specimens of *D. latum.*

B. Subgenus SPIROMETRA (with "Piled" Uterine Coils)

Diphyllobothrium houghtoni Faust, Campbell and Kellogg, 1929.

Synonym.—*Diphyllobothrium mansoni* (Cobbold, 1882) of Faust and Wassell,

cat in Peking The strobila is much smaller and more delicate than that of *Diphyllobothrium latum*, measuring in length from 85 cm. (human material) to 110 cm (canine material). The bothria are poorly developed and serve to form only a shallow sucking groove on either side of the scolex. The distalmost gravid proglottids are slightly broader than long, rectangular in outline, and measure 3 to 3 5 mm. in breadth by 2 7 to 3.2 mm in length. Both the vitellaria and testes are compactly distributed throughout the lateral fields, they encroach mesad on the uterine coils and coalesce in the anterior field to form a deep arch over the male genital opening. The l

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inner proximal coils of the uterus. There are four and a half to seven loops of the outer uterine tube, placed compactly on one another; they are equally broad except for the terminal loop which is more swollen in contour. The inner coils of the uterus, which contain the less mature eggs, are much smaller in diameter and form a compressed rosette. The eggs are ellipsoidal in shape, each with a rounded conical operculum, and measure 57 to 66 μ in length by 33 to 37 μ in transverse diameter

The life cycle of this species in unknown but the first intermediate host is probably a *Cyclops*, and the second intermediate host, some vertebrate in which the spar- itive host The

Pathogenesis, Pathology and Symptomatology.—Unstudied.

Diagnosis.—On the basis of finding the eggs in the patient's stool. These eggs can be readily differentiated from those of *D. latum* and *Diplogonoporus grandis*,

oleoresin of Aspidium

Control. This consists in abstinence from eating the raw flesh of animals harboring the sparganum stage of this worm

Diphyllobothrium mansoni (Cobbold, 1882) Joyeux, 1928. (Manson's tapeworm.)

Synonyms.– *Ligula mansoni* Cobbold, 1882; *Bothriocephalus liguloides* Leuckart, 1886, *Bothriocephalus mansoni* (Cobbold, 1882) Blanchard, 1888; *Dibothrium mansoni* (Cobbold, 1882) Ariola, 1900; *Sparganum mansoni* (Cobbold, 1882) Stiles and Tayler, 1902, *Plerocercoides mansoni* (Cobbold, 1882) Guiart, 1910, *Sparganum raillieti* v. Rátz, 1912; *Dibothriocephalus mansoni* (Cobbold, 1882) Manson-Bahr, 1925, *Diphyllobothrium erinacei* (Rudolphi, 1819) of Iwata, 1933, *pro parte*.

Historical and Geographical Data.—This tapeworm, first recovered by Manson in its larval stage in 1882 at the autopsy of an Amoyese, and commonly designated as "Manson's tapeworm," is frequently found in its adult stage in dogs and cats and their wild relatives in the Sino-Japanese area, extending as far south as French Indo-China This species has also been obtained from the cat in Puerto Rico (Cram, 1926) and at New Orleans, La Kouri (1944) states that in certain rural areas in Cuba 100 per cent of the cats are infected, although in urban communities the worm has not been found The adult stage is probably not infective for man (Faust, Campbell and Kellogg, 1929) On the other hand, the sparganum stage of this, and several closely related species has been found to be parasitic in man over a wide area in the Far East, the usual types of the infection being subcutaneous and ocular

sparganosis. Many hundreds of human cases are on record, including those from South China, Japan, Formosa, Netherlands Indies, and particularly Tonkin; the number of diagnosed cases with ocular sparganosis is on the increase in Tonkin (French Indo-China).

Structure of the Adult Worm.—The adult *Diphyllobothrium mansoni*, which is commonly a parasite of the small intestine of the dog, the wolf, the fox, the cat, the wild cat, the leopard and the tiger, resembles *D. latum* in its general appearance, but differs from the latter in being much more delicate in its structure and in seldom attaining a length of more than 60 cm. to a meter. The present author is in general agreement with Joyeux and Houdemer (1928) with respect to the points of specific differentiation of *D. mansoni*. The scolex measures 1 to 1.5 mm. in length by 0.4 to 0.8 mm. in breadth, is nearly quadrangular in transverse section and has the free margins of the bothria well developed. The proglottids are broader than long except at the distal end of the strobila, where they may be approximately square, and are somewhat smaller than those of *D. houghtoni*. The testes and vitellaria are situated in the lateral fields but occasionally coalesce anteriorly. The uterus describes three to five loops in its ascent from the oötype to the uterine pore. The three genital orifices are all in the median line. The vaginal pore is much nearer to the male orifice than it is to the uterine pore. The eggs vary considerably in size; they measure 52 to 68.5 μ in length by 32 to 43.5 μ in transverse diameter.

The sparganum stage of *D. mansoni* is much larger than that of *D. latum*. The range of second intermediate hosts is very great, comprising various species of frogs, snakes, birds and mammals, including man.

The Life Cycle of the Worm.—The life cycle of *Diphyllobothrium mansoni* essentially parallels that of *D. latum*, involving a eucopepod crustacean as first intermediate host, a vertebrate as second intermediate host, and a vertebrate as definitive host. The eggs (Fig. 141) are discharged from the parent worm and are passed in the feces. They require about five weeks in water to complete their maturity, whereupon they hatch and the ciliated hexacanth embryo (Fig. 142) escapes through the opened operculum, swimming through the water with a *Volvox*-like movement. In the event the embryo is ingested by an appropriate species of Cyclops, *Mesocyclops leuckarti* (Claus, 1857) G. O. Sars, 1918, Okumura (1919) has shown that it works its way into the body cavity of the Cyclops and becomes transformed into a procercoid larva. While the experimental data obtained by Okumura undoubtedly hold true for *D. mansoni*, it is not unlikely that this investigator was working with two or more species of *Diphyllobothrium*, including *D. decipiens* and *D okumurai*. Iwata (1933) who has been unable to differentiate these several species of the subgenus *Spirometra* one from the other, has concluded that they are all one species, which by the Law of Priority should be designated as *Diphyllobothrium erinacei* (Rudolphi, 1819). Joyeux, Houde[illegible] (1934) and the present author do not concur in [illegible] this opinion. [illegible] by Yokogawa [illegible] there is a group of several closely interbreeding species, [illegible] tinguishable, although with difficulty. Li (1929) has confirmed this work for *D. decipiens* and *D. erinacei* and has found that several Oriental species

of Cyclops are appropriate first intermediate hosts. If, then, the infected Cyclops is swallowed (in raw drinking water) by a frog, a snake, a bird or a mammal, the Cyclops is partially digested in the stomach of the host, the larva works its way out, penetrates through the stomach wall, and wanders along the peritoneal surface of the intestine, usually migrating to the deeper somatic muscles of the host, but at times lodging in the iliac fossæ, pleural cavity, the lumbar region (including the perirenal tissues), the urethra, etc. In these foci the larvæ (Figs. 143, 144) become metamorphosed into the sparganum type, which cannot be distinguished from the sparganum of *D. latum* except for its larger size. Here also it may multiply by budding, the number of asexual progeny being contingent only on the space and nourishment available. Bonne (1942) demonstrated experimentally that the proceroid stage of *D. ranarum*, an intestinal parasite of the cat in Java, when developed to maturity in local Cyclops, did not readily produce infection (*i. e.*, sparganum stage) in adult frogs or toads. However, when the infected Cyclops were fed to the tadpole stage of these amphibians, abundant infection was obtained. Similarly inoculation of the mature procercoids into mice and monkeys by the oral route produced sparganums in these

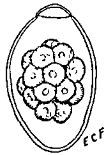

FIG. 141.—Egg of *Diphyllobothrium houghtoni* or *D. mansoni*. × 500. (Original.)

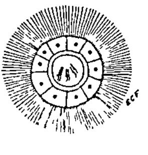

FIG. 142.—Free-swimming hexacanth embryo of *Diphyllobothrium mansoni* × 500 (Original.)

hosts. Frogs and snakes, which are universally infected with these sparganum larvæ throughout the Far East, are commonly consumed by dogs and cats and their wild relatives. As far as is known from experimental evidence, ingestion of the sparganum stage by an acceptable mammal always produces an intestinal and never a somatic infection. Otherwise the sparganum is digested.

Epidemiology.—In so far as is known, man is susceptible to infection with the *sparganum* stage only, although this may be acquired in one of at least two ways. It is reasonable to believe, but not proved, that man may acquire somatic or visceral sparganosis as a result of drinking raw water containing infected Cyclops. On the other hand, most of the many clinical cases observed in the Far East (French Indo-China, China, Japan) give a history of applying the flesh of the second intermediate host (usually a frog) as a poultice to an inflamed or suppurating surface of the body. (Joyeux and Houdemer, 1928; Faust, Campbell and Kellogg, 1929).

Pathogenesis, Pathology and Symptomatology.—(*a*) *The Adult Worm.*—Mature spargana of this species ingested experimentally by man have failed

to produce intestinal diphyllobothriasis (Faust, Campbell and Kellogg, 1929), although the adult worms are common in dogs and cats in endemic areas.

(*b*) *The Sparganum.*—The more common method of infection, and the only one definitely proved for man, is by application of the fresh flesh of a second intermediate host containing viable spargana to an injured member or tissue of the body. On contact with the warm human flesh the spargana migrate out of the poultice into the human tissues. A number of observations have been made on the presence of unbranched spargana in the human host. These record the condition produced by the mature larva in the

FIG 143 —Infection of *Sparganum mansoni* in *Natrix tigrina* Natural size (Original photograph)

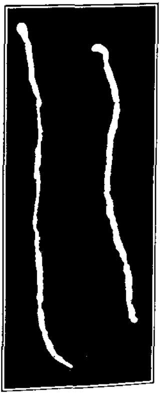

FIG 144 —Mature specimens of *Sparganum mansoni* from experimental infection in rabbits × 2 (Original)

somatic musculature, connective tissue, or in the region of the orbit. If infection is due to the ingestion of infected Cyclops, the number of larvæ is small, so that the migration of the larvæ through the stomach wall, and [illegible] for development [illegible] eases and [illegible] their channels in the subcutaneous tissue or muscle fascia become more and more extensive, the region assumes a "puffy" or edematous appearance and becomes very painful to the touch. Opening of the lesion reveals a slimy matrix, at times with a chylous exudate, within which the spargana are actively elongating and contracting, or in which they have degenerated into a caseous mass. Death of these larvæ provokes an intense local inflammatory reaction. Bonne (1932) reported the recovery of two unbranched spargana from an infarcted pulmonary artery of man, and Bonne

and Lie Kian Joe (1940), of a sparganum from the intestinal wall. Monkeys and pigs in Java are commonly infected with this same species of sparganum (*i. e.*, developing in the intestine of cats into *D. ranarum*). In 1947 the author identified a living unbranched sparganum obtained by Dr. I. A. Robins of Baton Rouge, Louisiana from the subcutaneous tissues of a native female white patient who sought assistance for a pruritic dermatitis.

The presence of the larvæ in the tissues in and around the eye (*ocular sparganosis*) is characterized by intense pain, irritation and edematous swelling of the eyelids, with excess lacrymation. Subconjunctival infection produces a toxemia of the area and, at times, nodule formation. Retrobulbar invasion leads to lagophthalmos and corneal ulceration. Fibrous connective-tissue formation around the parasites has not been observed.

Diagnosis.—This can be made only after opening the lesion and obtaining the characteristic unbranched sparganum larvæ, which are frequently attached to the tissue by their suckers They should be distinguished from *Sparganum proliferum* (Fig. 148), which is irregular in shape and usually branched. Those of the species *mansoni* (*sensu stricto*) can be differentiated from other unbranched forms [*D. decipiens* (Diesing, 1850), *D. erinacei* (Rudolphi, 1819), *D. ranarum* Meggitt, 1925, *D. reptans* Meggit, 1925, *D.*

hosts, and careful study of the adult worms recovered from the intestine of these experimental hosts.

Therapeusis.—This consists, wherever feasible, in removal of the spargana, draining and dressing the lesion. Cornet (1933) recommended the injection of 2 to 4 cc. of 40 per cent ethyl alcohol with novocaine (free of epinephrin) to kill the worms *in situ*. They may then be removed or be allowed to be absorbed. Keller (1937) successfully employed novarsenobenzol intravenously (30 to 45 cgms. per dose for adults, 7 to 15 cgms. for children) every four or five days for two to six administrations, for orbital infections. Tarsorrhaphy is considered desirable in ocular sparganosis to preserve the cornea until the worms are absorbed or are discharged in the dressing.

Prognosis.—Dependent entirely on the position of the parasite in the host's body and the ease with which it can be removed without injury to vital organs.

Control.—Boiling or filtering all drinking water in endemic areas; abstinence from swallowing live tadpoles, and avoiding the local application, to ulcers or inflamed areas, of frogs or other vertebrates infected with spargana.

Genus Diplogonoporus Lönnberg, 1892

(genus from διπλόος, double, γόνος, reproductive, πόρος, pore)

Diplogonoporus grandis (R. Blanchard, 1894) Lühe, 1899. (The double-pored giant tapeworm.)

Synonym. *Krabbea grandis* R. Blanchard, 1894

This double-pored pseudophyllidean tapeworm has been recovered six times from man, in each instance from Japanese patients The normal hosts are said to be

whales. The complete worm measures from 1.4 to 5 9 meters in length. The proglottids (Fig. 132, *12*) are broad and short, measuring from 15 to 25 mm. in breadth by 0.45 mm. in length. The genital pores and uterine openings are situated in paired ventral grooves lateral to the midline. The uterus of each of the two genital sets in each proglottid consists of only a few loops [illegible] (Fig. 145) are broadly ovoidal, dark brown [illegible] by 50 μ in cross-section. The life cycle is [illegible] second intermediate hosts [illegible]

Vergeer (1935) has discovered that *Diplogonoporus*-like proglottids may arise as a bifurcation of the genital primordia of species of *Diphyllobothrium*.

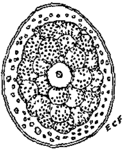

FIG. 145 —Egg of *Diplogonoporus grandis*. × 500. (Original)

Pathogenesis, Pathology and Symptomatology.—Colicky pains in the abdomen, progressive secondary anemia, accelerated pulse rate (120), lassitude, alternating diarrhea and constipation, are all common symptoms of the infection.

Diagnosis.—On the find [illegible] or a ribbon of t[illegible] passed in the st[illegible] purge.

Therapeusis.—*Oleoresin of Aspidium*, as indicated for *D. latum*

Control.—Unknown, but the history of one of the cases is suggestive of infection from salt-water fish

GENUS DIGRAMMA CHOLODKOWSKY, 1914

(genus from δίς, twice, and γραμμή, line or streak)

Digramma brauni (Léon, 1907) Joyeux and Baer, 1929.

Synonym.—*Diplogonoporus brauni* Léon, 1907.

Three specimens of this species of tapeworm (Fig 146) have been recovered from

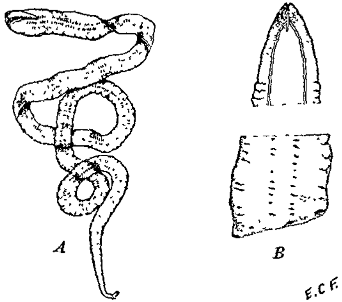

FIG 146.—*Digramma brauni*. *A*, complete worm, natural size, *B*, head and anterior end, × 4 (After Léon, in Brumpt, Précis de Parasitologie)

two patients in Roumania.
ribbon, measures only 12 cr
transverse rings and the scol
neck region is very inconspicuous. The genital openings, together with the genital apparatus for each proglottid, are paired Genital atria are said to be lacking. The

acquired by man as a result of eating raw, infected fish.

Pathogenesis, Pathology and Symptomatology.—Patients harboring this worm are said to suffer from anemia.

Diagnosis.—From the recovery of the strobila or ripe proglottids of the parasite in the stool.

Therapeusis.—*Oleoresin of Aspidium*, as indicated for *Diphyllobothrium latum*

Control.—Unknown, but the infection is probably acquired from consumption of raw fresh-water fish

Genus Ligula Bloch, 1782

(genus from *ligula*, tongue)

Ligula intestinalis (Goeze, 1782) Gmelin, 1790.

Synonym.—*Braunia jasseyensis* Léon, 1908.

This tapeworm, belonging to the subfamily **Ligulinæ** of the family **Diphyllo-**

patient. It is a fleshy, ribbon-shaped parasite (Fig. 147), measuring 18 to 20 cm. in length and 8 to 12 mm in breadth The scolex is triangular in shape and the two suckers possess shallow grooves There is no neck region. Externally the segmentation of the worm is hardly perceptible, but internally it is distinct. On both the dorsal and ventral sides there is a median longitudinal sulcus, extending the entire length of the worm. The ovary is branched, with a single median stem. The testes are arranged in two

(Fuhrmann, 1931). In the normal definitive host (various species of fish-eating birds) the worm becomes sexually mature in about two days It is only an accidental parasite of man

In a study of *L intestinalis* and related species of diphyllobothrids Smyth (1946, 1947, 1948) has been able to develop the worms aseptically *in vitro* in a peptone broth at 40°C., starting with the sparganum stage removed from the body cavity of infected fresh-water fishes until maturity and deposition of fertile eggs beginning about the seventh day of incubation This worker has concluded that metabolic stimuli resulting in the completion of development consist primarily in transfer from a relatively cool environment, such as exists in the aquatic fish host, to a warmer environment, such as that in the bird.

Fig 147 —*Ligula intestinalis* (syn *Braunia jasseyensis*) anterior end, natural size (After Léon in Brumpt, Précis de Parasitologie)

Pathogenesis, Pathology and Symptomatology.—"*Diarrhea and headache,*" as well as nausea and vomiting, are recorded symptoms.

Diagnosis.—From the recovery of the strobila in the stool.

Therapeusis.—*Oleoresin of Aspidium* is probably specific.

Control.—Unstudied. One patient was a fish merchant, suggesting raw fish as a source of infection.

LARVAL PSEUDOPHYLLIDEAN CESTODES OCCURRING IN MAN

Genus Sparganum Diesing, 1854

(genus from σπάργανον ribbon)

Sparganum mansoni. See *Diphyllobothrium mansoni* (above).

Sparganum proliferum (Ijima, 1905). (The proliferating sparganum.)

Synonyms.—*Plerocercus prolifer* Ijima, 1905; *Sparganum* (*Gatesius*) *proliferum* (Ijima, 1905), Stiles, 1908

This larval pseudophyllidean tapeworm was first recovered from the subcutaneous tissues of a woman living near Tokyo At least 5 other cases have been found in Japan and one (a fisherman) from Manatee, Florida. In 1948 the author diagnosed an additional case, that of extensive cerebral involvement in a Polish refugee who was necropsied in Prague by Professor Dr. Herman Šikl.

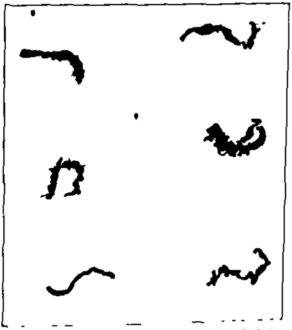

FIG 148 —*Sparganum proliferum* × 2 (Original photograph)

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the sparganum, and develop into new larvæ. Thus far ... have been unsuccessful.
S. proliferum is a branched variety of *S mansoni*

In the cases described the spargana were found by the thousands in the subcutaneous tissues and the intermuscular fasciæ, as well as in the walls of the ali-

mentary canal, mesentery, kidneys, lungs, heart and brain. Osseous tissues alone are apparently not invaded. On ingestion by experimental vertebrate hosts, the mature *S. proliferum* larvæ are digested, but on experimental transplantation into the subcutaneous tissues or peritoneal cavity of mammals they live and proliferate

The adult stage of the organism and its life cycle are unknown.

Epidemiology.—Unstudied

Pathogenesis, Pathology and Symptomatology.—Nothing is known of the migra-

[illegible]

indicate the almost unlimited potentiality of asexual multiplication The infection finally becomes so serious that the host tissue is transformed into honeycombed lesions (Fig 149), the presence of the parasites provoking nodule formation and attempts on the part of the host tissue to wall off the parasite At first the affected area is edematous and yields under pressure When involving lymph channels the infection may produce an elephantiasis of the member Opening of each of the nodules allows the escape of from one to several worms, together with a watery or chylous fluid Later, however, the cyst wall becomes thickened by the deposition of fibrous tissue, so that it is firm to the touch If the lesions are subcutaneous, the body may be covered with acneform pustules, which cause intense itching The deeper lesions produce less definite symptoms but are the more dangerous

Diagnosis.—On the expression of the characteristic larvæ from subcutaneous nodules of the infected individual.

Therapeusis.—The multiple lesions, usually involving the viscera as well as the somatic tissues, make treatment practically hopeless.

Prognosis —Grave, particularly where primary centers are involved

Control.—Unknown, since the life cycle of the organism is unknown

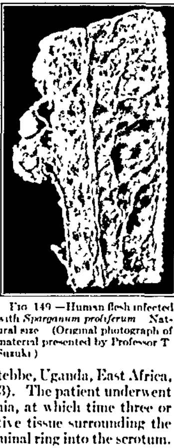

Fig 149 —Human flesh infected with *Sparganum proliferum* Natural size (Original photograph of material presented by Professor T Suzuki)

Sparganum baxteri Sambon, 1907.

This sparganum, which is morphologically indistinguishable from that of *Diphyllobothrium mansoni*, was removed by Baxter from an abscess in the thigh of a native in East Africa. It may be the same species as *Sparganum mansoni*, or a closely related form.

A second case of sparganosis, in a native of Entebbe, Uganda, East Africa, has been reported by de Meillon and Leech (1943). The patient underwent an operation for repair of a right inguinal hernia, at which time three or four small nodules were removed from connective tissue surrounding the spermatic cord as it passed from the external inguinal ring into the scrotum. One of the nodules contained a whitish sparganum 5 to 10 cm. long, and from another several pieces of sparganum were removed. There was no evidence of additional foci of infection in the patient.

Sparganum mansonoides (Mueller, 1935).

In 1935 Mueller described as a new species a *Diphyllobothrium* of the

subgenus *Spirometra*, which has been recovered in the United States from New York to Florida and west to Louisiana. The adult worms develop in the cat and less favorably in the dog, but the bob-cat is believed to be the important definitive host. Acceptable first intermediate hosts are species of Cyclops (*Megacyclops leuckarti*, *Mesocyclops viridis* and *Diacyclops bicuspidatus*), in the hemal cavity of which the procercoids develop. The sparganum or plerocercoid stage is found naturally in the water snake (*Natrix*) and in the field mouse (*Microtus*), and is expermentally infective for mice rats, rhesus monkeys, the ring-tailed monkey and leopard frogs, by oral feeding of the sparganum. In these animals the larvæ migrate through the intestinal wall to the muscles, where they reëstablish themselves. Rhesus monkeys are also susceptible to oral infection with the procercoid stage (Mueller, 1938).

In the rhesus monkey the presence of the spargana in the musculature provokes a fibrous tissue encapsulation, which tends to block lymph drainage, especially in the lower levels of the trunk, producing an elephantiasis of the dependent parts. In severe infections there is also a terminal edema. In most experimental hosts the sparganum infection provokes a 15 to 35 per cent eosinophilia. While there is no record of natural human infection with *Sparganum mansonoides*, the susceptibility of the monkey to oral infection with both the procercoid and sparganum stages of the worm "renders human infection very probable" (Mueller, 1938*a*), and experimental human infection has been demonstrated by Mueller.

Sparganum spp.

Three cases of sparganosis in man have been reported from Australia. Although two of these cases were reported as harboring *Sparganum mansoni* (*i. e.*, *Bothriocephalus mansoni vel liguloides*), Cleland inclines to the view that they are specifically different and that their normal host is a snake or monitor. Additional cases of human infection with unbranched spargana [illegible] (Ronne,
[illegible] 15)
[illegible] ına
[illegible]

is *sub judice*.

CHAPTER XVIII

THE CYCLOPHYLLIDEAN CESTODES

ORDER CYCLOPHYLLIDEA BRAUN, 1900

THE cestodes belonging to the Order **Cyclophyllidea** are characterized (1) by the presence of four symmetrically arranged cup-shaped suctorial pockets on the scolex, (2) by the lateral opening of the genital atrium,[1] (3) by the absence of a uterine pore, and (4) by the complete development *in utero* of the non-ciliated hexacanth embryo, which is housed in a non-operculate shell. The scolex is usually provided with an apical projection, the *rostellum*, which may or may not be armed with hooks All of the human cyclophyllidean tapeworms belong to the superfamily **Tænioidea** Zwicke, 1841, which is distinguished by having non-operculate eggs with one or more shell layers, non-ciliated oncospheres and four simple suckers arranged symmetrically around the scolex

Family ANOPLOCEPHALIDÆ Cholodkowsky, 1902

This family contains many species of mammalian tapeworms, having an unarmed scolex and large unarmed suckers, but lacking a rostellum and a neck region. The only species known to occur in man are *Bertiella studeri* and *B. mucronata*, two of the six species of this genus recorded from Primates.

GENUS BERTIELLA STILES AND HASSALL, 1902
(genus named for Dr. Paul Bert)

Bertiella studeri (Blanchard, 1891) Stiles and Hassall, 1902. (Bert's tapeworm)

Synonyms.– *Bertia satyri* Blanchard, 1891; *Bertia studeri* Blanchard, 1891; [illegible]

[illegible] *æthiops pygerythrus, C nictitans schmidti* and *Hylobates hoölock*, as well as from a dog in the Philippines Several human cases have been reported, including four in Mauritius (Blanchard, 1913, Adams and Webb, 1933, Adams, 1935), several others from India (Chandler, 1925, Mukerji, 1927, Maplestone, 1930, Roy, 1938), one from Deli, Sumatra (Joyeux and Dollfus, 1931), one from St Kitts, British W Indies (Cameron, 1929), and one from the Philippines (Africa and Garcia, 1935). Other species of *Bertiella* reported from macaques, baboons and the gibbon are possibly all referable to this species

Morphology, Biology and Life Cycle. The worm has a total length measurement of about 275 to 300 mm. and a maximum breadth of 10 mm. when relaxed. The subspherical head (Fig. 150 *A*) is distinctly set off from the neck. It measures 475 μ in transverse diameter. Apically there is a

[1] An exception is found in the genus *Mesocestoides* Vaillant, 1863, in which the genital openings are situated medially on the dorsal side

rudimentary unarmed rostellum. The conspicuous oval suckers measure 220 by 150 μ. The strobila at the insertion of the head has a transverse measurement of 275 μ but narrows down to 225 μ at a distance 2 mm. behind the head where segmentation begins.

The mature proglottid (Fig. 150 *B*), which contains a full complement of reproductive organs, measures about 6 mm. in breadth by 0.75 mm. in length. The genital pores alternate irregularly. The crescentic ovary lies on the side of the proglottid in which the genital pore is situated, as do the "shell gland" and the seminal receptacle. The majority of the numerous

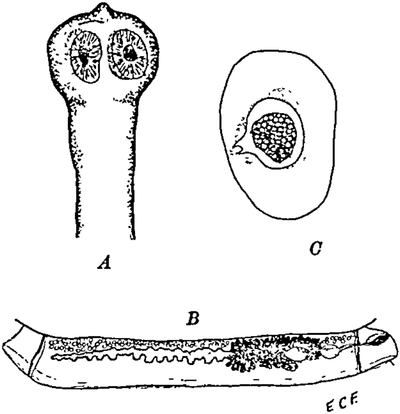

FIG 150.—*Bertiella studeri* *A*, head, × 52, *B*, mature proglottid, × 20, *C*, egg, × 600 (*A* and *B*, after Chandler, Journal of Parasitology, *C*, adapted from Blanchard)

testes are situated on the opposite side, while the uterus with its anterior and posterior lateral branches extends horizontally from the ootype towards the aporal margin As the proglottids become more and more gravid, the uterus comes to occupy an increasingly greater portion of each segment The testes and seminal receptacle, however, persist for a considerable time. Finally the uteri usurp practically all of the proglottids, which are shed in groups of about two dozen. The eggs (Fig 150 *C*) have an irregular, crinkled, oval outline, measuring 45 to 46 μ by 49 to 50 μ. The middle envelope is very delicate. The inner shell is dawn out on one side into a bicornuate apparatus. The life cycle of the worm is now known Direct feeding of the eggs to young macaques was not successful (Adams, 1935). As in the life cycle of *Moniezia expansa* (Stunkard, 1937), so in this infection certain species of mites serve as intermediate hosts (Stunkard,

1939, 1940). Eggs obtained from gravid proglottids, when fed to the mites *Schelonbates lævigatus* and *Galumna* sp , hatched and developed into cysticercoid larvae in the hemal cavity of the mite. The larvæ are spherical, ovoidal or pyriform, measure 0.1 to 0.15 mm. in diameter and possess a small cercomer. Accidental ingestion of the infected mite provides exposure for the mammalian host.

The related species, *Bertiella mucronata* (Meyner, 1895) Beddard, 1911, has been reported (Cram, 1928) as an intestinal parasite of man in Cuba, the patient having lived previously in the Canary Islands; likewise from a twenty-nine year old native worker in São Paulô, Brazil (Pessôa, 1930, 1938). This species is also recorded from the African chimpanzee (*Pan* sp), from *Cercopithecus* sp., from *Micetus niger*, and from the Paraguayan black howler (*Alouatta caraya*).

Epidemiology.—Unstudied.

Pathogenesis, Pathology and Symptomatology.—Unstudied.

Diagnosis—On recovery of the eggs with the irregular, oval outline and peculiar internal shell; or on obtaining chains of the characteristic gravid proglottids.

Therapeusis.—The worms are evacuated after administration of *oleoresin of Aspidium* or carbon tetrachloride, as prescribed for *Diphyllobothrium latum*.

Control—Unstudied.

Genus Inermicapsifer Janicki, 1910

(genus from *inermis*, unarmed, *capsa*, case, and *fero*, to carry)

Inermicapsifer cubensis (Kourí, 1939) Kourí, 1940

Synonyms.—*Raillietina cubensis* Kourí, 1939, *R. louridoralensis* Dollfus, 1939–1940; *R. loechesalavezi* Dollfus, 1939–1940

History and Geographical Distribution.—This tapeworm has been found to be endemic only in Cuba, mostly in the city of Havana and environs (Provinces of Habana, Matanzas and Pinar del Rio). The first case was discovered in 1935 and since that time there have been many dozen human infections diagnosed. Kourí (1944) states that there is possibly one valid record from Lara State, Venezuela

Morphology, Biology and Life Cycle.—The mature worm (Fig. 151, *1*) has a total length of 27 to 42 cm and contains 310 to 368 proglottids. The unarmed scolex measures 0 61 mm. in transverse section The four suckers protrude noticeably from the margin of the scolex; each sucker has a diameter of approximately 185 microns (Fig. 151, *2*, *3*). The neck has a length of about 3 mm. The mature proglottids (Fig. 151, *4*) are broader than long (2 3 by 1 5 mm.), while the more distal, gravid ones (Fig. 151, *6*) are longer than broad (3 to 3.75 by 1 to 2 mm.). Each proglottid is provided with a single reproductive system containing both male and female organs The genital pore and genital atrium are lateral in position, midway between the anterior and posterior planes of the proglottid. The cirrus pouch is 150 microns long and contains a muscular penis The vas deferens is long and tortuous In each proglottid it is possible to identify 33 to 49 small testes The ovary and vitellaria almost completely encircle the

oötype. In each gravid proglottid there are 48 to 175 mother egg capsules, each of which [illegible]

The [illegible] mediate host (Stunkard, 1941).

Epidemiology.—Very little epidemiological information is available. Infection has been found mostly in children from five to eleven years of age. All but one of seventy cases reported up to 1944 were white. The patient usually harbors a single parasite but occasionally there may be more than one. Kourí (1944) believes that man is not the optimum host but no natural reservoirs have been found.

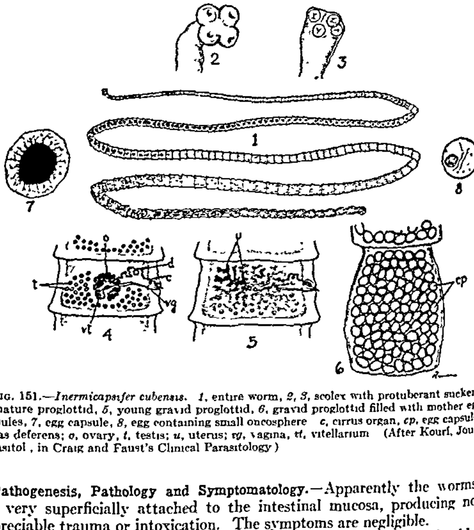

FIG. 151.—*Inermicapsifer cubensis.* *1*, entire worm, *2*, *3*, scolex with protuberant suckers; *4*, mature proglottid, *5*, young gravid proglottid, *6*, gravid proglottid filled with mother egg capsules, *7*, egg capsule, *8*, egg containing small oncosphere *c*, cirrus organ, *cp*, egg capsule, *d*, vas deferens; *o*, ovary, *t*, testis; *u*, uterus; *vg*, vagina, *vt*, vitellarium (After Kourí, Jour. Parasitol., in Craig and Faust's Clinical Parasitology.)

Pathogenesis, Pathology and Symptomatology.—Apparently the worms are very superficially attached to the intestinal mucosa, producing no appreciable trauma or intoxication. The symptoms are negligible.

Diagnosis.—This consists in recovery of the characteristic proglottids in the stool, or in discovering the entire worm passed spontaneously.

Therapeusis.—*Extract of Aspidium* and *carbon tetrachloride* have proven to be satisfactory in expelling the worms. At times they are passed spontaneously without anthelmintic medication.

Control.—This can not be undertaken until the epidemiology of the infection has been more adequately elucidated.

Family MESOCESTOIDIDÆ (Benham, 1901) Fuhrmann, 1907 emend. Byrd and Ward, 1943

This family of tapeworms is unusual among cyclophyllidean species in the following respects: (1) The genital atrium lies in the middorsal line rather than on the lateral margin of the proglottid; (2) there are two separate vitelline glands, (3) both pairs of longitudinal excretory tubules lie in the same dorso-ventral plane, and (4) the eggs in gravid proglottids are massed together within a para-uterine fibrous capsule. All described species of the family belong to the genus *Mesocestoides*. The species *M. variabilis* Mueller, 1928 has been reported as a human parasite.

Genus Mesocestoides Vaillant, 1863

(genus from μέσος, middle, κέστος, tape and εἶδος, similar)

Mesocestoides variabilis Mueller, 1928

Historical and Biological Data.—This species was first described by Mueller (1928) from the gray fox (*Urocyon cinereo-argenteus californicus*), the spotted skunk (*Spigale phenax phenax*) and the western skunk (*Mephitis occidentalis occidentalis*), all from California Mueller (*l. c.*) regarded the material from *M. occidentalis* as a variant and designated it as *M variabilis* var. *maior* Chandler (1942) reported this same tapeworm from a dog and a raccoon in Nebraska and East Texas, and Byrd and Ward (1943) described it from the opossum (*Didelphis virginiana*), in Mississippi. Chandler (1942) reported this same species from a white child, 13 months of age, who had been treated for tapeworms by Doctor Henry Tucker, of Nacogdoches, Texas.

Morphology and Life Cycle.—The co-type specimens of this species (Mueller, 1928) vary in length from 5 to 8 cm, are about 1 mm. in maximum width and contain approximately 400 proglottids The scolex is small, is well differentiated from the neck and is provided with relatively large, deeply excavated suckers. Chandler (1942) has described the material from man In this collection there were four scolices but no intact strobila. The estimated total length of a complete strobila is 40 cm., the maximum width, 1.5 to 1.8 mm., with a total of about 400 proglottids. The scolices (Fig 152, *A*) measure 0.47 to 0.6 mm. in breadth by about 0.35 to 0.4 mm in length and are separated from the neck by a distinct constriction. The neck is approximately 7 to 10 mm. long; the mature proglottids, 1.0 to 1.4 mm. broad, and the gravid ones, 1.7 to 2.5 mm. long by 1.25 to 1.6 mm. broad.

Except for some of the testes all of the genitalia in both the mature and gravid proglottids of *M. variabilis* lie medially to the pair of inner (main) longitudinal excretory canals (Figs. 152, *B*, *C*). The genital pore (*gp*) is median dorsal, about one-third of the proglottid's length from its proximal end, internally the genital pore leads into a flask-shaped atrium. There are 15 to 55 testes (*t*) on each side of the mature segment; they are arranged more or less in broad masses ventral to the main excretory canal A single vas efferens (*ve*) arises from the mid-region of each group of testes and

proceeds medially to a position immediately anterior to the ovary, where it joins its mate from the opposite side to form a dilated vas deferens (*vd*). After convoluted looping this common tubule enters the cirrus sac (*c*) and is continued as the dilated seminal vesicle (*sv*) which opens into the genital atrium. The muscular cirrus organ, which is surrounded by prostate glands, is the outer prolongation of the seminal vesicle. The ovary (*ov*) is bilateral and each lobe is somewhat constricted medially; it is situated in the posterior part of the proglottid. A short oviduct, arising from the isthmus of the ovary, proceeds posteriorly into an oöcapt (*oc*). A pair of vitelline glands (*vit*), situated slightly lateral to the outer portion of each ovarian lobe, discharge yolk cells which are carried in transverse ducts (*vit d*) to the mid-line behind the oöcapt. There they fuse and proceed as

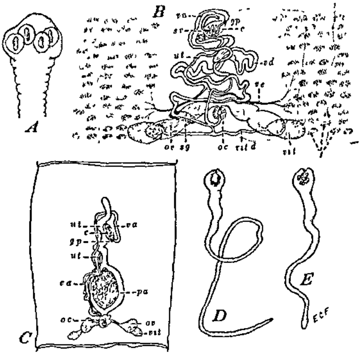

Fig. 152.—*Mesocestoides variabilis* *A*, scolex, with four suckers, × 8 *B*, portion of mature proglottid, greatly enlarged, showing the genitalia, *C*, gravid proglottid, greatly enlarged, showing the parauterine organ with mass of eggs, *D*, *E*, mature second larval state (*tetrathyridium*) of *Mesocestoides* sp., showing the long sparganum-like tail and the scolex invaginated into the somewhat bulbous anterior extremity *c*, cirrus sac, *gp*, genital pore; *oc*, oöcapt, *ov*, ovary, *pa*, parauterine organ, *sg*, Mehlis' gland, *sv* seminal vesicle; *t*, testis, *ut*, uterus, *va*, vagina, *vd*, vas deferens, *ve*, vas efferens, *vit*, vitellarium, *vit d*, vitelline duct. (Original adaptations, *A*, from Mueller, *B*, *C*, from Byrd and Ward, *D*, *E*, from Witenberg)

a common duct, to join the duct arising from the oöcapt and the vagina before opening into the uterus. The vagina (*va*) has a rather convoluted course from the genital atrium to its junction with the common vitelline duct. Mehlis' gland (*sg*) surrounds the inner end of the uterus. The uterus (*ut*) loops several times before arriving at a blind terminus in the vicinity of the genital pore. In the gravid proglottid, a swollen, thick-

longitudinal plane, measuring 400 to 530 microns in length by 320 to 365 microns in diameter, and contains an egg mass nearly filling the reservoir. The individual eggs in the capsule are ovoidal, measuring 24 to 26 by 20 to 22 microns. The exact method by which the eggs escape has not been described but it seems likely that this occurs on rupture of the capsule.

The life cycle of *Mesocestoides* is very imperfectly known. Viable eggs, evacuated from the definitive host and escaping from gravid proglottids, serve as a source for infection of the first intermediate host (as yet unknown but believed to be an arthropod). In this host the oncosphere probably migrates out of the midgut into the hemocelic cavity and develops into a first stage larva, which is as yet unknown. On ingestion of the infected first host a second intermediate host (various species of reptiles, amphibia, birds and mammals) acquire the infection and the organism develops into the second larval stage in the extra-intestinal tissues. This larva is the *tetrathyridium*, a plerocercus type with a somewhat bulbous anterior end containing an invaginated head with four suckers (Fig. 152 *D, E*). It measures from a few to many millimeters in length. If the appropriate definitive host eats the infected tissues of the second intermediate host, the worm develops in about two weeks into the mature strobila in the small intestine of this host. However, if the third host is not entirely suitable for the worm, the infection may be lost, the worm may develop much more slowly or never mature, or it may migrate into extra-intestinal tissues and remain in the tetrathyridium stage. In this respect its development is similar to that of species of *Diphyllobothrium*, subgenus *Spirometra* (*vide supra*).

Epidemiology.—Very little is known about the way in which the definitive host acquires the infection, but available evidence suggests that it is due to eating the tissues of the second intermediate host containing the tetrathyridium-stage larva. Human infection is incidental in the propagation of the life cycle.

Pathogenesis, Pathology and Symptomatology.—The single human infection reported was in an infant, thirteen months old, who had been ill for two to three months, was suffering from poor appetite, "pain in the stomach," loss of weight and was passing long ribbons of tapeworm.

Diagnosis.—This is based on demonstration of the characteristic gravid or mature proglottids in the stool.

Prognosis.—Unstudied

Therapeusis.—*Oleoresin of Aspidium* has been demonstrated to be relatively specific for this infection.

Control.—Unstudied

Family DILEPIDIDÆ Fuhrmann, 1907, emend. Lincicome, 1939

This cyclophyllidean family of tapeworms is characterized by having suckers armed or unarmed, a rostellum, when present, provided with hooklets, and a uterus more or less sacculate or ramified, either breaking up into many oviferous capsules or provided with a para-uterine organ which receives the eggs. The family contains one species, *Dipylidium caninum*, which is from time to time a human parasite.

Genus Dipylidium Leuckart, 1863

(genus from δίs, two, and πυλίs, gate)

Dipylidium caninum (Linnæus, 1758) *Railliet, 1892.* (The double-pored dog tapeworm, causing dipylidiasis or dog tapeworm infection.)

Synonyms.– *Tænia canina* Linnæus, 1758, *pro parte; Tænia moniliformis* Pallas, 1781, *Tænia cucumerina* Bloch, 1782; *Tænia acteniformis* Goeze, 1782 *pro parte; Tænia elliptica* Batsch, 1786, *Tænia cuneiceps* Zeder, 1800; *Dipylidium cucumerinum* (Bloch, 1782) Leuckart, 1863, probably also *D. canicum* Lopez-Neyra, 1927; *D. caracidoi* Lopez-Neyra, 1927; *D. cati* Neumann, 1896; *D. compactum* Milzner, 1926; *D. crassum* Milzner, 1926, *D. diffusum* Milzner, 1926; *D. gracile* Milzner, 1926; *D. halli* Tubangui, 1925; *D. longulum* Milzner, 1926; *D. porimamillanum* Lopez-Neyra, 1927; *D. sexcoronatum* v. Rátz, 1900; *D. walkeri* Sondhi, 1923. In addition, the genera *Alyselminthus* Zeder, 1800, *Halysis* Zeder, 1803, and *Microtænia* Sedgwick, 1884, [illegible]

Historical and Geographical Data.—This common tapeworm of the dog is also frequently found in the cat, the wild cat, (*Felis silvestris*) the jungle cat (*Felis catus constantina*), *Felis catus ocreata*, the Indian palm cat (*Paguma leucomystax grayi*), the civet cat, the hyena, the jackal, the dingo, the fox, and from time to time in man. Blackie (1932) found this worm together with *Hymenolepis diminuta* in a native girl in Southern Rhodesia It is reported sporadically as a human parasite in Moravia (Kučera and Jirovec). The author has diagnosed it three times in New Orleans children and Sunkes and Sellers (1937) in a four-year old boy in Atlanta, Ga.

Structure and Life Cycle.—The worm, which lives in the small intestine, consists of a strobila composed of elliptical proglottids and measures from 100 to 500 mm. in length. The head (Fig. 153*A*) is small, rhomboidal, has a transverse diameter of 300 to 400 μ, and possesses four deeply-cupped, ovoidal suckers and a median, anterior, club-shaped rostellum, the latter being capable of protrusion to a length of 185 μ or of complete invagination into the head. The rostellum is armed with 3 to 7 circlets of spines, each of which has a short, curved arm and a large, rounded base. The anterior series are the largest and the posterior ones the smallest. The neck is short and slender. The immature proglottids range from those that are shorter than broad to those that are squarish. The mature proglottids (Fig. 153*B*) are longer than broad and begin to assume the characteristic pumpkin-seed shape. They are provided with a double series of reproductive organs, with a genital pore on each lateral margin. Receptacula seminis are lacking. The gravid proglottids are distinguished by the unique character of the uterus which has the appearance of a polygonal block work through the median field of each segment.

In each uterine pocket there is a group of 8 to 15 eggs enclosed in a mother embryonic membrane (Fig. 153 *C*). The eggs (*Fig. 153 D*) are spherical, measure from 25 to 40 μ in diameter and are usually tinged a delicate brick-red, which gives a reddish color to the gravid proglottids. The delicate hooklets measure 12 to 15 μ in length. The gravid segments become separated singly or in groups of two or more from the parent worm

and frequently wander out through the anus. Their disintegration in the bowel or, later, on the ground, liberates the groups of eggs which are usually found within the intact mother envelope.

The eggs are ingested by the larval stages of ectoparasitic insects, particularly the dog flea, *Ctenocephalides canis*, the cat flea, *C. felis*, and the human flea, *Pulex irritans*, which frequently lives on the dog. The dog louse, *Trichodectes canis*, has also been incriminated as a suitable host of *Dipylidium*, although Zimmermann (1937) considers that the species is not *D. caninum* and Stewart (1939) states that it is *D. sexcoronatum*.

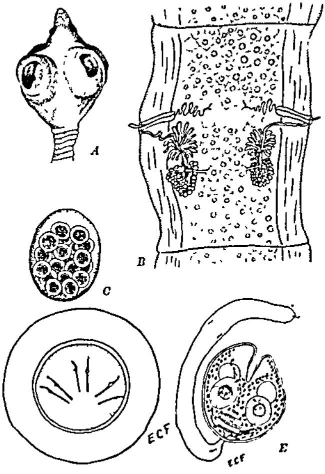

FIG. 153 *Dipylidium caninum* *A* scolex, greatly enlarged, (adapted from Stiles). *B*, mature proglottid, enlarged (original), *C*, egg cluster in embryonic membrane (after Stiles) *D*, single egg × 1000 (original). *E*, cysticercoid larva, greatly enlarged, (after Grassi and Rovelli in Braun-Seifert, Die tierischen Parasiten des Menschen)

If Venard (1938) is correct in regarding *D. sexcoronatum* as a synonym of *D. caninum*, then *T. canis* must be listed as an arthropod host of *D. caninum*. Grassi and Rovelli found that the eggs hatch out in the gut of the insect and penetrate into its hemal cavity, where they become metamorphosed into cysticercoid larvæ (Fig. 153 *E*). These larvæ mature in this location and are transferred to the mammalian host when the adult

insect is accidentally ingested. More recently Chen (1934) has studied the complete history of [illegible] how amebocytes and ot[illegible] flea frequently attack the young worms and destroy them. The high mortality of fleas during the migration of the young cysticercoids through the flea larva's intestinal wall and later during the *pupal stage of the insect* is apparently due to damage caused by the tapeworm larvæ. On digestion of the parasitized insect in the intestine of the mammal the cysticercoid is liberated, attaches itself to the intestinal mucosa, and completes its development.

The infection in dogs and cats is cosmopolitan. In man several hundred cases are known from Germany, Denmark, Italy, Switzerland, Norway, Sweden, Austria, Holland, France, England, the United States, Colombia (one record, Patiño Camargo, 1940), Mexico (in an infant forty days old, Cervantes, 1940), the Philippines, Japan and China. Most of these human infections have been reported from children.

Epidemiology.—Human beings who have harbored *Dipylidium caninum* almost invariably give a history of close association with dogs or cats which are worm-infected and flea-infested. Exposure is probably due to swallowing fleas infected with the mature larval stage of the worm.

Pathogenesis, Pathology and Symptomatology.—Dogs and cats may harbor large numbers of the worms without appreciable symptoms except emaciation and colic. Human beings are seldom infected with more than a single worm. In small children, who are most commonly parasitized, slight intestinal disturbances and toxic nervous symptoms may develop.

Diagnosis.—On the basis of finding the gravid proglottids in the stool or migrating out of the anus; or the finding of clusters of eggs in the stool.

Therapeusis.—*Oleoresin of Aspidium*, as administered in *Diphyllobothrium latum* infection (p. 266). In two patients who harbored this parasite, the present author advised the use of tetrachlorethylene, 3 minims per year of age, with preceding and post-treatment saline purgation. Follow-up examinations were negative.

Control.—Human infection usually results from accidental ingestion of the infected insect hosts while fondling dogs or cats infested with these ectoparasites. This is particularly true for small children, who are the most common group infected with this species.

Family DAVAINEIDÆ Fuhrmann, 1907

This family consists of several genera which are parasitic in the digestive tract of birds and mammals. Its members are characterized by having numerous minute hooklets on the margins of the suckers as well as two or three rows of hammer-shaped hooks on the rostellum. Representatives of several species of *Raillietina* have been recorded from man.

GENUS RAILLIETINA FUHRMANN, 1920
(genus named for Professor A. Railliet)

Raillietina madagascariensis (Davaine, 1869) Joyeux and Baer, 1929 (The Madagascar tapeworm)

Synonyms.—*Tænia madagascariensis* Davaine, 1869; *Davainea madagascariensis* (Davaine, 1869) Blanchard, 1891. [Joyeux and Baer (1929) state that the specimens

referred to as "*Davainea madagascariensis*," even from the type locality, belong to more than one species, all of which they place in *Raillietina*]

Historical and Geographical Data.—First discovered by Grenet in children at Mayotte in the Comoros, several cases of human infection with this worm are now known, including 1 case from [illegible]

norvegicus, 8 62 per cent in *R rattus*)

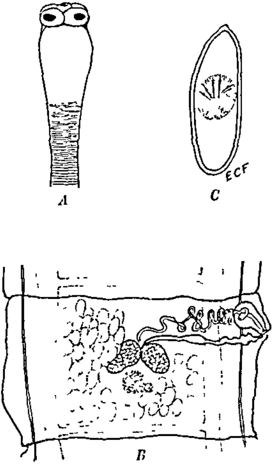

FIG 151 *Raillietina madagascariensis* A head greatly enlarged (after Blanchard, in Brumpt, Précis de Parasitologie) B mature proglottid × 40 original adaptation (from Garrison) C mature egg × 600 (adapted from Garrison).

Structure and Life Cycle. The worm is 24 to 39 cm. long and very narrow, with a maximum breadth of 2.6 mm. The scolex (Fig 151A) has four deeply excavated, closely set, cup-shaped suckers, while crowded between them at the anterior end of the head is a cushion-shaped rostellum provided with about 90 to 110 hooks set in two rows. There is a marked constriction between the head and the body, but no neck region. The anterior unsegmented portion of the worm is slightly broader than the head. There

are altogether from 500 to 700 proglottids. The immature ones are very narrow, the mature ones about one and a half times as broad as long, and the gravid ones nearly twice as long as broad. Each proglottid (Fig. 154*B*) contains only one set of reproductive organs, the genital pore being situated laterally near the proximal margin. A receptaculum seminis is present. The uterus consists of a mass of coiled tubules, which completely fill the entire gravid proglottid. These coils are crowded with 120 to 150 mother capsules, each enclosing one to three eggs. The eggs (Fig. 154 *C*) are elliptical or spindle-shaped, measure 50 to 64 μ by 19 to 23 μ, and each contains an oncosphere measuring 8 to 15 μ in diameter. The latter has *three pairs of lancet-shaped hooklets.*

The life history of the organism is unknown but it is believed that cockroaches of the genus *Periplaneta* serve as intermediate hosts

Epidemiology. Unstudied.

Pathogenesis, Pathology and Symptomatology.—Unreported.

Diagnosis.—Based on the recovery of the characteristic proglottids or eggs

Therapeusis.—*Oleoresin of Aspidium* is probably effective.

Prophylaxis.—Unstudied.

Raillietina celebensis Janicki, 1902. (The Celebes tapeworm.)

Synonyms.—*Davainea formosana* Akashi, 1916; *Raillietina formosana* (Akashi, 1916) Joyeux and Baer, 1929.

Biological and Geographical Data.—This species has been reported from a patient in Tokyo, Japan, and from one in Formosa. Its reservoir host is the rat. It differs from *R madagascariensis* in being somewha[illegible] ...correspond-ingly larger number of segments (more than [illegible] suckers, and in having a larger number of [illegible] containing at most four eggs. The eggs are also much larger (99 by 40 μ), while the oncosphere is 12 by 14 μ in diameter. The life cycle of the worm is unknown. The exact status of this specimen remains *sub judice.*

Epidemiology.—Unstudied

Clinical Data.—Nothing is known of the clinical history of the persons infected, except that one worm was passed spontaneously after administration of calomel

Raillientina (?) asiatica (v. Linstow, 1901) Stiles and Hassall, 1926.

Synonyms.—*Tænia asiatica* v. Linstow, 1901; *Davainea asiatica* (v. Linstow, 1901) Braun, 1903

The specimen, on which this doubtful determination was made, consisted of a worm, with about 750 proglottids but without head, obtained from a case in Ashabad, Northern Iran. The egg capsules numbered 60 to 70 The size of the many eggs crowding each capsule is not stated

Raillietina demerariensis (Daniels, 1895) Dollfus, 1939-1940

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(1922) from nine patients (5 women, one man and 3 children) out of 194 examined in the vicinity of Quito, Ecuador. León (1935) described the Ecuadorean worms as new (*R. quitensis*), while Dollfus (1939) created three new species from material sent him by León. According to Kourí (1944) all of these tropical American Raillietinas should be regarded as one species, *R. demerariensis*.

Thus far *R. demerariensis* has been reported from British Guiana (Daniel's one case), Ecuador (Alvarez Crespo, 1944 states that León found 5 per cent incidence in the population of Machachi, in the environs of Quito) and in Cuba (3 cases, reported by Kourí and Doval, 1938 as *R. madagascariensis*).

Structure and Life Cycle.—One of Daniel's specimens had a length of 23 cm. and possessed about 320 proglottids León's specimens measured up to 10 to 12 meters in length by 3 mm in breadth. The suckers are ovoidal, less than 0 5 mm in diameter and are engirdled by a row of persistent hooklets. Apically the scolex has a retractile rostellum, with a double corona of hooklets. There are approximately 5,000 proglottids, of which the less mature ones are squarish (2 mm) and the gravid ones are longer than broad (3 5–4 0 × 3 mm.). On separation from the strobila the gravid proglottids assume the shape of a rice grain Each ripe proglottid had 75 to 250 polygonal egg capsules, which, on becoming free from one another, assume a spherical contour about 200–250 μ in diameter. Each capsule contains several eggs (7 to 9, rarely fewer or at times as many as 12) The eggs are ovoidal to subspherical, measure 25 to 40 μ in greater diameter and contain conspicuously large hooklets.

The life cycle of this parasite has not been elucidated.

Epidemiology.—Essentially unstudied. In the environs of Quito this is a relatively common infection of man.

Diagnosis.—This is based on recovery of the characteristic gravid proglottids evacuated from the bowel

Clinical Data.—It is reported that the patients are seriously affected by this parasite, experiencing abdominal pain, nausea, flatulence, diarrhea, vertigo, severe headache and mental dullness. Excellent results were obtained in Ecuador following the administration of calomel purgation and *extract of Aspidium.*

Control.—Unstudied

Family HYMENOLEPIDIDAE Railliet and Henry, 1909

This family contains a very large number of species occurring in the intestinal tract of birds and mammals The worms have proglottids usually broader than long The uterus is sac-like and persistent. The majority of the species have an insect as intermediate host, but a few species require only the vertebrate in which to complete the entire life cycle. The species reported from man are *Hymenolepis nana*, *H. diminuta* and *Drepanidotaenia lanceolata*.

Genus Hymenolepis Weinland, 1858

(genus from ὑμήν, membranous, and λεπίς, shell)

Hymenolepis nana (v. Siebold, 1852) Blanchard, 1891. (The dwarf tapeworm, causing hymenolepiasis nana or dwarf tapeworm infection.)

Synonyms.—*Tænia murina* Dujardin, 1845 (*nec* Gmelin, 1790); *Tænia nana* v. Siebold, 1852; *Tænia ægyptiaca*, Bilharz, 1852; *Diplacanthus nanus* Weinland, 1858; *Hymenolepis fraterna* Stiles, 1906.

Historical and Geographical Data.—The dwarf tapeworm of man was discovered by Bilharz, in 1851, in the small intestine of a boy who had died of meningitis in Cairo. Since that time it has been found to be fairly cosmopolitan in its distribution, although it is perhaps more common in warm than in cold climates, and is much more frequently a parasite of children than of mature individuals. It is the most common human tapeworm in the Southern United States. The following percentage incidence of infection has been reported from Latin American countries: Argentina, 0.7 to 9.0; Brazil, 5.91; Colombia, 0.38, Costa Rica, 1.38; Cuba, 0.07; Chile, 0.17 to 0.99; Ecuador, 4.35 to 6.94; Haiti, 0.16; Nicaragua, 7.0; Mexico, 0.62 to 16.2; Ven-

It is fre-

t of the

Pacific islands but it rarely occurs in Guam. Stoll's estimate of world incidence (1947) is 20.2 million persons, mostly in the U. S. S. R. and Asia. The common dwarf tapeworm of the rat and the mouse (*Hymenolepis nana* var. *fraterna*), is morphologically indistinguishable from *H. nana* of man but is physiologically different, so that the murine form produces infection normally only in rats or mice and the human form normally only in the human host.

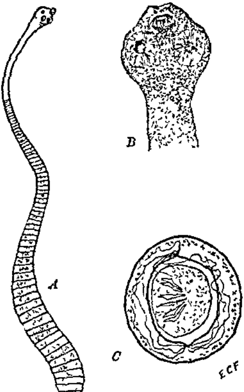


Fig. 155 —*Hymenolepis nana* *A*, complete strobila, × 10 (original), *B*, head, greatly enlarged (after Blanchard, in Brumpt, Précis de Parasitologie), *C*, egg, × 466 (after Joyeux, in Brumpt, Précis de Parasitologie)

Structure of the Adult Worm.—The entire worm (Fig. 155*A*) has a length measurement of only 25 to 40 mm, while its maximum diameter does not usually exceed 1 mm. In general the size of the strobila is inversely proportional to the number of worms present in the host. The rhomboidal head (Fig. 155*B*) has a transverse measurement of about 0.32 mm., is provided with four hemispherical suckers 80 μ in cross-section, and has a short rostellum armed with a single circlet of 20 to 30 spines The neck is long and slender. The most proximal proglottids are very short; those successively more mature are longer and larger, reaching a maximum

...out 0.15 to 0 3 mm. in length by

, C) are spherical or subspherical,

nd, in addition to the vitelline

membrane, have two membraneous shells, the inner one of which has two polar thickenings, from each of which there arise from 4 to 8 long thread-like filaments. These filaments are easily seen in viable eggs but are more difficult to demonstrate in preserved material. The enclosed oncosphere measures 16 to 19 μ in diameter. The three pairs of hooklets of the onco-

sphere are lancet-shaped. The terminal proglottids either begin to disintegrate while still attached or drop off from the worm one by one and disintegrate, so that the eggs are recovered individually from the stool.

The Life Cycle of the Worm.—The life cycle of *Hymenolepis nana* was first studied by Grassi and Rovelli (1887, 1892), who fed gravid proglottids of the rat parasite to uninfected rats and found successive states of development in this host, until, on the thirtieth day, eggs appeared in the stool. These experiments, showing that no intermediate host was required for the complete development of the parasite, were later confirmed by Joyeux (1920) and Woodland (1924). On the other hand, Bacigalupo (1931) has provided experimental evidence that certain fleas (*Ctenocephalides canis*, *Xenopsylla cheopis* and *Pulex irritans*), as well as certain beetles (*Tenebrio molitor* and *T. obscurus*), are capable of serving as intermediate hosts and transmitting agents of the murine variety of this worm in Argentina.

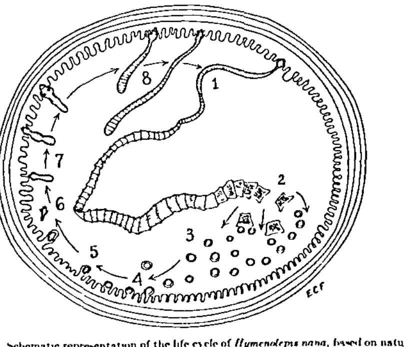


FIG. 156. Schematic representation of the life cycle of *Hymenolepis nana*, based on natural infection in a mouse. *1*, complete strobila attached to mucosa of ileum by its scolex, with *2*, disintegrating gravid proglottids. *3*, eggs set free by *2* either pass out in feces, are taken into the mouth as a contamination and are swallowed, or, without leaving the small bowel, hatch and *4*, the liberated hexacanth embryos invade the villi and develop into *5*, larvae with scolex provided with suckers and rostellar booklets like adult strobila. *6*, larvae escape from villi and *7*, *8*, becoming attached to villi, develop into *1*, adult strobilae. (Original.)

The usual life cycle, which is illustrated in figure 156, involves ingestion of eggs recently passed in the feces, their hatching in the duodenum, penetration of the freed oncospheres into the stroma of the duodenal or jejunal villi and their transformation into the larval stage (*cercocystis*), escape of the cercocysts into the lumen of the small bowel, their attachment to the mucosa and development in about two weeks into mature strobilae. (Grassi and Rovelli, 1889, 1892, Joyeux, 1920, Woodland, 1924, Hunninen,

1935). Thus, man serves both as the larval and definitive host and only a single individual is employed in a full life cycle.

Grassi first sponsored the view that the rat and human species were identical, basing his view on the infection of one out of 6 children who were fed gravid proglottids of the parasite in the rat. Saeki (1920), whose work was confirmed by Uchimura (1922), succeeded in infecting rats and mice, as well as a monkey and a child, aged four years, with eggs from the human host, although he was not able to infect himself. Kiribayashi (1933) has also infected children with eggs from a murine strain, and has discovered no essential morphological difference between worms from the two strains. Woodland's results (1924), in infecting mice (7 out of 30) with eggs from a child's stool under carefully controlled conditions, also support the identity of the human and rat varieties. These experiments indicate that reciprocal infections can be accomplished and probably do occur at times in Nature Working with two murine strains in rats and mice, Shorb (1933) found that there was an initial resistance to infection during the nursing period, which, however, was soon lost; that there was a gradually developed age resistance, and that there was definite resistance to superimposed infection. Shorb also discovered that an inadequate diet reduced resistance to infection. Furthermore, these two murine strains were physiologically as different from one another as they were from the human strains.

Epidemiology.—Except for possible human infections acquired from murine sources, man is the source of his own dwarf tapeworm infection. Without question the usual transmission is a direct hand-to-mouth contamination, as Keller, Leathers and Bishop (1932) have demonstrated for Tennessee, where they found an average incidence of 2.9 per cent in an examination of 31,999 individuals and a maximum incidence of 3.6 per cent in the 5 to 9 year group. In a heavily infected aborigines population in Formosa, Mazeozoko (1935) found 28.6 per cent of the children between two and five years old parasitized by this worm, 44.6 per cent of the six to ten year group, 10.7 per cent of the eleven to fifteen year group and 3.6 per cent or less for the older groups. Keller and Leathers (1934), in a survey of 44 [illegible]
with 0.5 per [illegible]
tina Castex . [illegible]
in Buenos Aires infected, while Bacigalupo (1932) reported a [illegible] incidence in children of the same city. There is a tendency for the incidence of infection to be higher and the worm burden higher in children within a family or in an asylum than in the general population of the same age group in the community. Occasionally there is fairly convincing circumstantial evidence that internal reinfection is taking place.

Eggs freshly discharged from the bowel have been found to be at the optimum stage of viability.

Pathogenesis, Pathology and Symptomatology.—Although *Hymenolepis nana* is the smallest of the human tapeworms, it may give rise to severe nervous or generalized toxic symptoms, particularly in small children or when the parasite is present in large numbers. In heavily infected patients, abdominal pain, with or without diarrhea, convulsions, epilepsy, insomnia and dizziness are recorded, and eosinophilia is quite a constant accompani-

ment (8 to 16 per cent). In patients with only a few worms there are usually no clinical manifestations (Wang, 1938)

Diagnosis.—This is based on the presence of the characteristic eggs in the stools.

Therapeusis.—*Oleoresin of Aspidium* (as recommended for *Diphyllobothrium latum*) is specific for this infection Goriacheva (1944), working in Samarkand, Turkestan, in an area where 26.2 per cent of the children between three and fourteen years of age were positive for *H nana*, recommends *extract of Aspidium* 0 5 Gm per year of age or 6–8 Gm. for adults. The anthelmintic is divided into three doses and is administered at ten-day intervals On the morning of treatment the patient is conditioned with a drink of one per cent sodium bicarbonate and one to one and one-half hours after treatment takes a saline purge. Reportedly 56.2 per cent of the patients remained free of eggs for one and one-half years.

Crystoids anthelmintic, in hard gelatine capsules, frequently gives very satisfactory results and is essentially non-toxic The patient is advised to take a light meal the night before treatment, to omit breakfast on the morning of treatment and to abstain from food for five hours subsequently. The dosage for a child of preschool age is 0 4 to 0 6 Gm., for an older patient, 1 Gm. Post-treatment saline purgation is helpful

Probably the transuodenal intubation of an emulsion of hexylresorcinol, as described by Brown (1948) and by Hernández-Morales and Santiago-Stevenson (1949) will prove to be more efficient than administering this drug orally as crystoids anthelmintic.

Berberian (1946), in Lebanon, employed an acridine derivative, *Acranil*, for treating 25 children parasitized with *H nana*. Each child was prepared with calomel purgation. Those between the ages of four and eight were given two 0.1 Gm. tablets in the morning on an empty stomach, with sodium sulfate purgation three hours later; then, for three consecutive days, one 0.1 Gm. tablet of the drug after breakfast For the eight to ten year group the dosages were three 0.1 Gm tablets the first morning and one 0 1 Gm. tablet morning and evening for three days, for the eleven to fourteen year group, four 0.1 Gm. tablets the first morning and one 0.1 Gm. three times a day for three days, and for two girls, fourteen and sixteen years old, five 0.1 Gm. tablets the first morning and one 0.1 Gm three times daily for three days The drug produced no serious by-effects. One week later 96 per cent, of the patients remained free, and two weeks later, 92 per cent, as indicated by stool examination. Infection thereafter increased to 48 per cent (five months after treatment), but reinfection could not be ruled out after the first two weeks.

Control.—The ability of the parasite to propagate itself without the intermediary of a secondary host and the ease with which it develops in children pose serious problems for the physician In crowded dwellings the infection is frequently contracted directly by one individual from another. Furthermore, it seems probable that a lightly infected individual is not only a *carrier* but reinfects himself so that he may come to harbor a number sufficiently large to produce symptoms. Malnutrition reduces resistance to infection or superimposed infection. Although the human infection is, in most cases, probably of human origin, infection from rodent

hosts is also a possibility. The development of habits of personal cleanliness in young children, particularly at toilet and with the hands, should be reflected in reduced incidence of this infection.

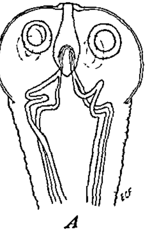
Hymenolepis diminuta (Rudolphi, 1819) Blanchard, 1891. (The rat tapeworm.)

Synonyms.—*Tænia diminuta* Rudolphi, 1819; *Tænia leptocephala* Creplin, 1825, *Tænia flavopunctata* Weinland, 1858; *Tænia varesina* Parona, 1884; *Tænia minima* Grassi, 1886.

Historical and Geographical Data.—*Hymenolepis diminuta*, the common cestode parasite of the rat and the mouse and other murine species, as *Praomys tullbergi jacksoni*, *Grammomys surdaster* and *Apodemus sylvaticus*, is an occasional human parasite. Asada (1923) also recovered it once from a dog. In certain areas, as in India, the U. S. S. R., Japan, Italy, and some of the Southern United States (including Tennessee, Georgia and Texas), this worm has been identified on several occasions. Moreover, its distribution is probably more widespread than has been suspected. Thus far nearly 200 authentic human cases have been diagnosed from Argentina, Brazil, Ecuador, Mexico, Cuba, Granada, Martinique, Nicaragua, Belgium, Italy, East Africa, the U. S. S. R., Japan, India, the Philippines, and from Arkansas, California, the District of Columbia, Georgia, Indiana, Louisiana, Minnesota, Nebraska, North Carolina, Oklahoma, Tennessee, Florida, Texas and Virginia.

Structure and Life Cycle.—The mature strobila measures 20 to 60 cm. in length and is definitely ribbon-like, increasing gradually in width from 0.5 mm. at the neck to 3.5 or 4.0 mm. at the distal end. It may consist of a thousand or more proglottids. The head (Fig. 157*A*) is small and rounded and is provided with four small, deeply excavated suckers and a median, anterior, invagination cavity, into which the unarmed, pyriform rostellum is usually retracted. The proximal proglottids are very short but the successively more distal ones are longer, the terminal ones measuring 0.75 mm. in length by 2.5 mm. in breadth. The mature proglottids (Fig. 157*B*) possess only three ovoidal testes. The genital pore is median lateral in position and alternates irregularly. The gravid proglottids become detached from the strobila, are partially digested, and the liberated eggs are set free into the lumen of the intestine. These eggs (Fig. 157*C*) are ovoidal in shape and have an outer measurement of 60 to 79 by 72 to 86 μ. The internal membrane, *i. e.*, that of the oncosphere, is provided with a thickening at each pole, but lacks polar filaments. Between the two membranes there is a colorless, elastic, gelatinous substance. The oncosphere measures 18 by 30 μ and has three pairs of lanceolate hooklets, arranged in a fan-shaped pattern. The eggs are intrinsically hyaline, but are usually stained a light greenish-yellow or yellowish-brown. They are relatively resistant to desiccation, to chemicals, and to putrefying agents (being viable for two months in feces), but are very sensitive to heat (60° C. or more). The adult worm lives attached to the anterior portion of the ileum [illegible] Among these [illegible] imago), *Tinea* [illegible] are [illegible] nd imago) and *granella*, *T. pellionella*, *Aglossa dimidiata* (both [illegible] two diplopods, *Aphornia gularis*; the ear-wig, *Anisolabis annulipes*,

Fontaria virginiensis and *Julus* sp ; the rat fleas, *Nosopsyllus fasciatus*,[1] *Orchopeas wickhami*[1] and *Xenopsylla cheopis*,[1] the mouse flea, *Ctenopsyllus segnis*;[1] the dog flea, *Ctenocephalides canis*,[1] the human flea, *Pulex irritans*;[1] the coleopterans, *Akis spinosa*, *Scaurus striatus*, *Tenebrio molitor* (larva), *Dermestes peruvianus*, *Geotrupes stercorsus*, *Tribolium castaneum*, *Ulosonia parvicornis*, *Aphodius distinctus* and *Stegobium paniceum*, and the cockroaches, *Periplaneta americana*, *Blatta orientalis* and *Blattella germanica* In the gut of these hosts the oncosphere hatches by the mechanical activity of its six hooklets (Vanni, 1938), penetrates through the intestinal wall into the hemal cavity, and becomes metamorphosed into a cysticercoid larva. On ingestion of the insect host by the definitive host the cysticercoid



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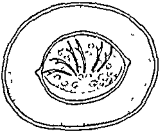


C

B

FIG. 157 *Hymenolepis diminuta* A, head, greatly enlarged showing suckers apical invagination cavity and proximal excretory tubules in a slightly compressed, living worm (original), B mature proglottid showing male and female organs greatly enlarged (adapted from Zschokke, in Stiles Hyg Lab Marine Hosp Bull No 25) C, egg × 580 (original)

becomes liberated, attaches itself to the intestinal wall and develops to maturity.

Addis and Chandler (1944) have provided important information concerning the vitamin requirements of *H diminuta* in the rat Some portion of the "G complex" in the hosts' diet is essential for normal growth Without vitamin A, as in Ackert's (1931) studies on *Ascaridia* in chickens and Burlingame and Chandler's observation on *Moniliformis moniliformis* in the rat, the partial paralysis of the bowel wall enriches the flora and increases the size of the worm The ratio of adult strobilae to the number of cysticercoid larvae ingested depends on the number of scolices which evaginate, become attached to the intestinal mucosa and mature Lack of "G complex" produces fewer attachments

[1] Infected of necessity during the larval stages

Epidemiology.—Man becomes infected after accidentally swallowing insects or other arthropod hosts which have previously become infected from consuming the eggs of the worm passed in feces of the murine host. Multiple infections up to nineteen strobilæ have been reported.

Pathogenesis, Pathology and Symptomatology.—Similar to other tapeworm infections. *Cachexia is not an uncommon accompaniment in multiple infections.*

Diagnosis.—Based on the presence of the characteristic eggs in the stool.

Therapeusis.—The worms are at times evacuated spontaneously or after a cathartic. *Oleoresin of Aspidium* is a specific anthelmintic.

Control.—Human infection may result from the accidental ingestion of infected insects living in cereals, such as flour or meal. Cold cereal breakfast foods, particularly when infested with the meal moth or meal worm, are subject to suspicion (Chandler, 1922). *In other cases man may become* infected from swallowing the ectoparasites of the murine host.

Genus Drepanidotænia Railliet, 1892

(genus from δρέπανον, lancet, and *tænia*, tape)

Drepanidotænia lanceolata (Bloch, 1782) Railliet, 1892. (The lanceolate tapeworm, causing drepanoteniasis.)

Synonyms.—*T* [illegible] *lanceolata (Bloch, 1782)* Weinland, 1858, [illegible]

This species is [illegible] *platyrhyncha*, *An* [illegible] *ferina*, etc.). The single human infection known was reported by Zschokke in 190[illegible] from a German youth, aged twelve years, who spontaneously evacuated two specimens. The worm has a length measurement of 5 to 13 cm. and a maximum width of 5 to 18 mm. The head is globular and small, has four deeply hollowed suckers and a cylindrical rostellum armed with a circlet of 8 lanceolate spines, measuring 31 to 35 μ in length. The eggs are ovoidal in contour, measure 50 by 35 μ, and have three envelopes, of which the innermost has polar papillæ. The inter- [illegible]

parasite in man is probably unstable.

CHAPTER XX

THE CYCLOPHYLLIDEAN CESTODES (CONCLUDED)

Family TÆNIIDÆ Ludwig, 1886

THIS family contains the most important tapeworms infecting man and domestic animals. The worms, either in their adult or larval stage, are usually large, the adult being a parasite of the intestine of carnivora or omnivora, and the larva or bladderworm (cysticercus, strobilocercus, cœnurus or echinococcus) developing in herbivora or omnivora. The testes are multiple; the uterus has a median stem with lateral arms. The outer egg-shell is thick, dark brown in color, and is composed of many minute, truncated pyramids cemented together.

GENUS TÆNIA LINNAEUS, 1758

(genus from *tænia*, tape)

Tænia solium Linnæus, 1758 (The pork tapeworm, causing tæniasis solium or pork tapeworm infection.) (According to Leuckart, the specific name "*solium*" is said to be derived from a Syrian term "*schuschl*," meaning a chain, which has come down through the Arabic word "*susl*" or "*sosl*," and has been turned into Latinized form, thus having no connection with the Latin word "*solus*," or single.)

Synonyms.—*Tænia cucurbitina* Pallas, 1766, *Tænia pellucida* Goeze, 1782; *Tænia vulgaris* Werner, 1782, *Tænia dentata* Batsch, 1786; *Halysis solium* (Linn., 1758) Zeder, 1803, *Tænia armata humana* Brera, 1808.

Historical and Geographical Data.—Although this species was not differentiated from *Tænia saginata* until the time of Goeze (1782), there is unquestionable evidence that it was known to the ancient Greeks. Aristophanes and Aristotle described the larval or bladder-worm stage (*Cysticercus cellulosæ*) from the tongue of swine and likened these larvæ to hailstones. Gessner (1558) and Rumler (1588) first reported human infection with the larval stage. Kuchenmeister (1855) and Leuckart (1856) first elucidated the life cycle and proved that human infection with the adult worm resulted from eating pig flesh containing the viable larvæ.

Infection with this worm is cosmopolitan, it is common wherever raw or inadequately cooked or processed pork is consumed by man. Possibly its highest incidence is found in the Slavic countries, Czechoslovakia (0.5 per cent incidence of intestinal infection, according to Kučera and Jírovec) and Jugoslavia, although Pavlov (1941) has shown a steady decrease in swine cysticercosis in Bulgaria since 1937. It is less prevalent in Germany than it was a half century ago. Intestinal and visceral infection with *T. solium* is encountered from time to time in North China and Manchuria. In India, especially in the Madras Presidency and in Calcutta, swine cysticercosis is extensive, although human infection is not heavy except in the outcasts (Hargreaves, personal communication). Evidence is accumulating of widespread distribution of the pork tapeworm in Latin America, from

Mexico to Venezuela and Ecuador. However, it is uncommon in Argentina (Dickmann, 1946). In Mexico the larval stage (cysticercosis cellulosae) "disputes with tuberculosis the privilege of occupying the first position among the causes capable of originating certain syndromes of intercranial hypertension" (Robles, 1946). Mazzotti (1944) reports that 2 per cent of over 4,000 stools examined in Mexico contained *Tænia* eggs (for the most part those of *T. solium;* that 4.34 per cent of 128, 025 hogs slaughtered in a little over two years were measled and that 2.9 per cent of 450 autopsies in Guadalajara revealed cysticercosis. In Ecuador Rodriguez (1944) reports 8.3 per cent intestinal infection vs. 0.7 per cent for *T. saginata.* Stoll (1947) has estimated the total world incidence of *T. solium* at 2 5 million persons, primarily in Africa, the U. S. S. R. and Asia. This figure appears to be ultraconservative.

Structure of the Adult Worm.—*Tænia solium* is the common human representative of the subgenus *Tænia,* which contains all of the species of the genus having an armed rostellum. The adult stage is known to develop only in man. The larval stage (cysticercus) commonly occurs in the pig, occasionally in man and other primates, and rarely in sheep and dogs. (Iwanizky states that 33 records of *Cysticercus cellulosæ* infection in dogs are found in the literature; Sandground, 1933, reported an additional canine infection from Yucatan, and Mazzotti, 1944, one from a dog and one from a cat in Mexico, D. F.) Apparently the same species of cysticercus has also been found in *Cercopithecus cephus, C. patas* and *Macaca sylvanus.* The adult is found attached to the anterior two-fifths of the small intestine It attains a length of from two to several meters. The scolex (Fig. 158), which is well buried in the intestinal mucosa of the infected host, is roughly quadrate, measures about 1 mm in diameter, and in addition to the four-cupped suctorial pockets, has a rostellum provided with a double row of alternating large and small hooks numbering from 22 to 32, and measuring 160–180 μ and 110–140 μ respectively. The suckers are slightly protuberant and measure up to 0 5 mm. in diameter. Rarely the scolex is pigmented In living specimens the neck has only about one-half the trans-sectional measurement of the head. The immature proglottids are broader than long, the mature proglottids are usually squarish, and the gravid proglottids are longer than broad, although never so conspicuously so as those of *Tænia saginata.* Althogether the number of proglottids is somewhat less than a thousand

Malformed proglottids are not uncommon; these usually consist of fenestrations or triangular proglottids intercalated among normal ones. Rarely triradiate forms have been observed, consisting of six suckers, a proportional increase in the number of hooklets, and three half-proglottids arranged more or less in [illegible] *T. saginata*

The mature proglottid [illegible]
(Fig. 162) and differs onl[illegible]

The testes are multiple follicular bodies, numbering 150 to 200 and distributed throughout the dorsal portion of the unit. Minute capillary vasa efferentia, with their inner termini connected with the follicles, join in dendritic fashion directly to form a common vas deferens, which proceeds as a convoluted tubule from the mid-plane transversely to the genital

atrium on the lateral margin, becoming enlarged distally into a cirral organ, containing prostate and cirrus elements. The genital atrium opens through a genital pore which possesses a powerful sphincter. The genital openings alternate irregularly from one side to the other in successive proglottids

Immediately posterior to the vas deferens is the vagina, which curves broadly posteriad towards the oötype. The ovary, which lies in the posterior part of the proglottid, consists of three lobes, namely a symmetrical pair of large lobes and an accessory lobe on the side of the genital pore The vitellaria consist of minute follicles, situated in a narrow elliptical band behind the ootype, at the posterior margin of the proglottid. The common vitelline duct and the vagina join the oviduct and proceed to the ootype, which is surrounded by "shell glands" The uterus arises from the anterior

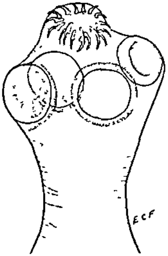


FIG. 158

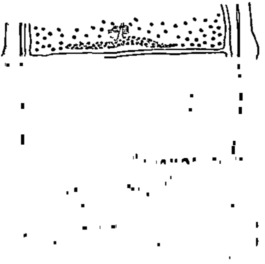


FIG. 159

FIG. 158 —Head of *Tænia solium* × 40 (Original adaptation of photomicrograph by Szidat, 1934, from Craig and Faust's Clinical Parasitology)

FIG. 159 —Mature proglottid of *Tænia solium* × ca 9 (From Faust after Leuckart, Parasiten des Menschen, courtesy of Akademische Verlagsgesellschaft)

face of the oötype. At first (Fig 159) it is a club-shaped sac, extending to the anterior border of the proglottid, but as it becomes filled with eggs, lateral extensions or arms develop and th to form the characteristic gravid uteru f primary arms is 7 to 13 (usually 9), a value, since the gravid segments of *T saginata* have no less than 15 (usually 18 or more) such lateral evaginations

The terminal gravid proglottids of the worm from time to time become separated either singly or in small groups from the strobila and are capable of independent movement, even to active migration outside the anus Either before separation, or later, the uterus becomes so distended with mature eggs that it bursts open along the median ventral line and the eggs escape. These eggs (Fig. 160) are spherical or subspherical in shape, measure 31 to 43 μ in diameter, are pale buff in color, and cannot be distinguished from those of *T. saginata* (Maplestone, 1937) The shell, which

is a thick-walled structure, made up of many truncated prisms cemented together, is originally provided with an outer mother embryonic membrane. According to Yoshino (1934) these embryonic envelopes may occasionally have one or two filamentous extensions. Between the envelope and shell there is a colloidal albuminous layer. Within the egg shell proper there is a fully-developed oncosphere, with its three pairs of hooklets, only occasionally clearly distinguishable through the shell (At times more than 6 hooklets are found. Yoshino (*l. c.*) reported as many as 18.)

Fig 160 —Egg of *Tænia solium*. × 666. (Original)

The Life Cycle of the Worm.—The eggs become freed from the uterus and their mother embryonic envelopes either before or after passing out in human feces. Their subsequent history involves their ingestion by the intermediate host, in the duodenum or jejunum of which the composite shells are broken down and within twenty-four to seventy-two hours the emergent hexacanth embryos penetrate the intestinal wall by use of their hooklets, pass through the blood stream or the lymph channels and settle down typically among the muscles, where they become metamorphosed into cysticerci. These latter reach maturity in sixty to seventy days. This stage (Fig. 161) is characterized by having a head similar to that of the adult, with fully-formed hooklets, invaginated into a broad, ovoidal bladder, which is grossly opalescent when alive (Fig. 162) and gives the "measly" appearance to the infected hog's flesh. The cysticercus, which

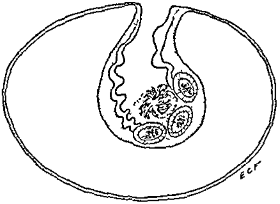


Fig 161

Fig. 162.

Fig 161 —Cysticercus of *Tænia solium*, showing scolex invaginated into bladder. Greatly magnified (Original)

Fig. 162 —*Cysticercus cellulosæ* within adventitious outer cystic capsule, removed from biceps muscle of man Natural size (Original photograph)

measures about 5 mm. in length by 8 to 10 mm. in breadth, is known as *Cysticercus cellulosæ*. From time to time man becomes infected with the cystericercus stage of *T. solium*. Cases are also known where the human subject with a history of intestinal tæniasis becomes infected with the cysticercus, it [illegible] suggests the possibility of internal autoinfection [illegible] æ may be single or multiple. [illegible] communication)

found two or more *Tænia* worms in 10 per cent of 200 intestinal infections, including 6 per cent with *T. solium* alone or with mixed *T solium* and *T. saginata*. The organs and tissue most commonly involved are the subcutaneous tissues, the brain (Fig 163), the orbit or the eyeball itself, the muscles, the heart including its valves, the liver and the lungs

Epidemiology.—Man readily acquires the intestinal infection through consumption of raw or inadequately cooked infected pork. He develops cysticercosis cellulosæ as a result of accidentally or unknowingly swallowing eggs of the worm (harbored by himself or someone else) passed in feces, or due to the precocious hatching of eggs discharged by an adult worm which he himself nurtures.

Upon passing into the lumen of the stomach the infective-stage cysticercus is digested out of its fleshy matrix, the bladder of the worm is digested away, and the uninjured head passes into the small intestine, where it evaginates and becomes attached to the intestinal wall. It then develops into the adult worm in about three months. The adult worm may live as long as twenty-five years in the human intestine

Pathogenesis, Pathology and Symptomatology.—*A The Adult Worm* —The worm lives in the small intestine, its head strongly anchored in the mucosa, the terminal (gravid) proglottids breaking off singly or in groups and passing out in the stool. Usually only a single worm is harbored at any one time. Ordinarily the parasite produces no grave clinical symptoms. At times, however, it may be responsible for vague abdominal discomfort, hunger pains, chronic indigestion with persistent diarrhea or with alternating diarrhea and constipation. In persons of a nervous temperament or in children the symptoms are at times more specific, consisting of anorexia, hyperesthesia, indigestion due to abnormal secretion of the intestinal juices, and various nervous complications It is believed that these disturbances are due to the absorption of toxic products of the worm. In rare cases it has been reported that the worm may perforate the intestinal wall and initiate peritonitis.

An eosinophilia up to 13 per cent or higher has been recorded for some cases. There is a moderate leukocytosis at the time when gravid proglottids are first discharged; later a moderate leukopenia is characteristic In chronic cases a secondary anemia may develop.

B. The Cysticercus.—Cysticercosis cellulosæ is not a unique condition in man. It has been known since 1558 As stated above, the larvæ may develop from viable eggs introduced into the intestine as an accidental contamination of food or drink, from soiled fingers, or as an internal autoinfection in a person who has previously become infected with the adult worm. The cysticerci of this species have been found in practically every organ and tissue of the body. The symptoms vary according to the number and exact position of the larvæ in the invaded tissues. They have been found most frequently in the subcutaneous tissues and in the brain, where they may reside in the ventricles or in superficial cysts in the meninges or arachnoid tissues. Clinically this latter variety of the bladder-worm is known as *Cysticercus racemosus* (Fig. 163). Next in the order of frequency they occur in the orbit, the musculature (Fig 162), the heart, the liver, lungs, abdominal cavity, etc.

Invariably in man the cysticercus is surrounded by a fibrous capsule, which is separated from the parasite by a space but is excised by the surgeon along with the larva. Th
vokes a typical sequence of local cel
of polymorphonuclear leukocytes,
and, at times, giant cells. Finally, fibrosis and necrotic changes of the capsule occur, and the parasites become calcified (Ch'in, 1933).

The more recent clinical studies on human cysticercosis (MacArthur, 1934; Dixon and Smithers, 1934; Chung and Lee, 1935) indicate the frequent occurrence of epilepsy in patients harboring cysticerci. *In case of internal auto-infection,* these symptoms may precede or be sequelæ to the

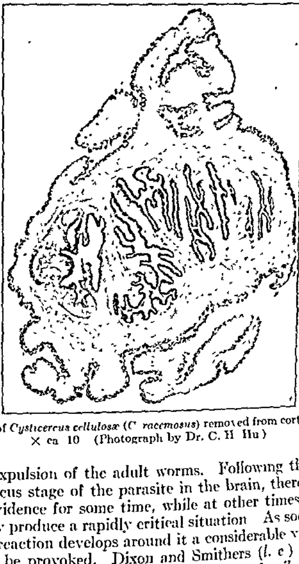


Fig. 163.—Section of *Cysticercus cellulosæ* (*C. racemosus*) removed from cortex of human brain × ca. 10. (Photograph by Dr. C. H. Hu.)

diagnosis and expulsion of the adult worms. Following the lodgment of the pre-cysticercus stage of the parasite in the brain, there may be little symptomatic evidence for some time, while at other times blockage of a passageway may produce a rapidly critical situation. As soon as the larva dies and tissue reaction develops around it a considerable variety of brain symptoms may be provoked. Dixon and Smithers (*l. c.*) state that "in every case of epilepsy occurring in a patient with no family history of fits and no previous history of fits in childhood, the possibility of cysticercosis should be entertained," while Dixon and Hargreaves (1945) add that cysticercosis should be considered wherever there is evidence of a brain tumor with an associated eosinophilia in the circulating blood and in the

spinal fluid. However, epilepsy is not a necessary accompaniment of cerebral cysticercosis (Edwards, 1946).

Elsæsser (1944), reporting 8 new cases and reviewing 63 earlier ones with a specific diagnosis of cerebral cysticercosis, has classified the symptoms under the following categories: (1) Those associated with adult hydrocephaly, *viz.*, early persistent headache, especially occipital or at the back of the neck, giddiness, nausea, vomiting, and the head is usually held rigidly to one side (Bruns sign); (2) mental dullness, often euphoria; (3) paranoia, depression and hyperesthetic emotional states; (4) papillary edema and (5) paresis of the third and sixth cranial nerves, cerebellar ataxy, and epilepsy, especially in the basal meningeal type. The history reveals that symptoms may develop suddenly or may have been noted up to thirty years. Relapse may occur after twenty symptomless years.

Many hundreds of cases of this infection are on record from Central Europe. During the first half of the nineteenth century 2 per cent of the human autopsies in Berlin showed these cysticerci. With the reduction of the adult infection in man and of the larvæ in pigs the incidence of human cysticercosis in Europe has become less frequent, but in Africa, India and China, where sanitary conditions are still very poor, cysticercosis is today not uncommon, and in Mexico, as stated above, it is a major clinical problem. Mazzotti's (1944) review of hospital records in Mexico demonstrates that 25 per cent of 100 cerebral tumors which came to operation proved to be due to *Cysticercus cellulosæ*, while 2.8 per cent of the recent autopsies in the Capitol City was afflicted with ocular cysticercosis.

Diagnosis.—*A. The Adult Worm.*—The presence of *Tænia* eggs in the stool does not permit of specific diagnosis, although in countries like Mexico it is relatively pathognomonic. Mazzotti (1944) regards perianal swabbing as an efficient method for rapid dispensary diagnosis. Recovery of gravid proglottids enables the diagnostician to determine without question whether the worm is *T. solium* or *T. saginata*. In the former case the lateral arms of the uterus are thirteen or less (Fig. 132, *2*), in *T. saginata* they number fifteen or more (Fig. 132, *1*). For immediate diagnosis the proglottids may be placed between two microscopic slides, pressed flat and examined against a strong light, or the uterus may be injected with India ink, whereupon it stands out in sharp contrast to the ivory-colored mesenchyma of the segment.

B. The Cysticercus.—Except in geographical regions where cysticercosis cellulosæ is common in man, specific diagnosis of human infection is usually deferred until after the larvæ have been excised and examined. Lumbar, cisternal or cerebral puncture occasionally reveals fragments of the cyst and 2 to 3 per cent eosinophils. Many of the cerebral type are located in the fourth ventricle and these are particularly dangerous if they grow forwards and block the aqueduct. At times radiological evidence reveals calcified cysts but only a small proportion of cerebral cysticerci studied by Dixon and Hargreaves (1945) were visualized by *x*-ray. Hargreaves (1945) has demonstrated that high penetration *x*-rays show up cysticerci in the brain in considerable detail, with the cyst wall appearing as a delicate shell around the calcified scolex. In the majority of cases diagnosis is never made unless the patient comes to necropsy. Pessôa and

his associates (1927, 1929) have demonstrated that aqueous extract of both *Cysticercus cellulosæ* and *C. bovis* provides positive intradermal and complement-fixation tests for patients infected with *C. cellulosæ*. The precipitin test is also positive. The cysticerci may be present singly or in multiples up to several hundred. Since immature, mature and degenerating or calcified cysts may be found simultaneously, there is reason to believe that continued or successive infections may develop in the same patient. In superficial tissues, excision is frequently indicated to confirm diagnosis; where the cysticercus is lodged in vital centers, as, for example, in the brain, its presence may be inferred only from *x*-ray shadows, varying in size from 1 to 23 mm. in length by 1 to 7 mm. in width and exhibiting a great variety of shapes (MacArthur, 1934). Cysticercosis of the brain must be differentiated from echinococcosis of the brain or embolisms of [illegible] s. A history [illegible] at a clinical [illegible] creased.

Therapeusis.—*A. The Adult Worm.*—*Oleoresin of Aspidium*, as administered in *Diphyllobothrium latum* infection, is usually a satisfactory anthelmintic. For good results the drug should be fresh. Rarely death may result from administration of this drug (Hernández Morales, 1945). *Carbon tetrachloride*, as utilized in hookworm infection is recommended by Carman (1929), Maplestone and Mukerji (1931), Sandground (1938) and other workers. Since there is cumulative evidence that many cases of human cysticercosis result from auto-infection, it is imperative that patients with intestinal tæniasis solium be specifically diagnosed as early as possible and that the worms be removed expeditiously and, if possible, without producing vomiting during the administration of the therapeutic.

While hexylresorcinol, administered by mouth in hard capsules (*i. e.*, crystoids anthelmintic), has very low efficiency in eradicating Tænias, the transduodenal intubation of an emulsion of this drug has been shown to be very effective (Brown, 1948; Hernández-Morales and Santiago-Stevenson, 1949). Moreover, Neghme and Faiguenbaum (1947) found atabrine to be very satisfactory in eliminating *Tænia solium*, *T. saginata* and *Hymenolepis nana*.

B. The Cysticercus.—Excision, wherever possible. Where the bladder-worm is lodged in vital centers, only symptomatic treatment is at times possible.

Prognosis.—*A. The Adult Worm.*—Usually good. After expulsion of the worm, the symptoms entirely disappear, although cysticercosis may develop as a sequela.

B. The Cysticercus.—Grave, except where the larva may be easily removed. Larvæ in inoperable sites in the body may calcify in the course of several months, or may die, but tissue reactions around those located in the brain and spinal cord frequently produce much graver symptoms than do the living cysticerci.

Control.—This involves both personal hygiene and sanitary measures. The former includes the abstinence from eating raw or rare pork except from carefully inspected slaughter-houses, and the greatest of care in handling the feces of persons known to harbor the adult *Tænia solium*.

Eggs of *T. solium* can apparently develop into cysticerci without passing outside of the body, so that this possibility must also be considered. Individuals harboring the adult worm should be relieved of their infection as soon as possible. Government inspection of "measly" pork has been primarily responsible for the marked reduction of both the adult and larval infection in man in Europe and the United States. According to Newsholme (1927) provisions were instituted in England as early as 1582 against the sale of "mesell pork," punishment for disobedience of the regulation consisting of a fine or the pillory. Rigid inspection should be instituted in all countries where the infection is not now under control and examination of pork should be extended to country slaughter-houses where the large city abattoirs are now under supervision. The present methods of pickling and smoking pork are not usually lethal to the cysticerci. Chilling is also not effective but freezing renders them non-viable. Cooking at 65.5° C. for several hours is believed to be lethal for the cysticerci (Hygiene Dept., British Royal Army Medical College, 1935).

Tænia saginata Goeze, 1782. (The beef tapeworm, causing tæniasis saginata or beef tapeworm infection.)

Synonyms.—*Tænia solium* Linnæus, 1767 *pro parte*, *Tænia cucurbitina* Pallas, 1781 *pro parte*; *Tænia inermis* Brera, 1802, *Tænia dentata* Nicolai, 1830, *Tænia lata* Pruner, 1847, *Tænia mediocanellata* Kuchenmeister, 1852, *Tænia zittaviensis* Kuchenmeister, 1852. *Tæniarhynchus mediocanellata* Weinland, 1858; *Tænia tropica* Moq.-Tandon, 1860, *Tænia (Cystotænia) mediocanellata* Leuckart, 1863.

Also, *Tænia abietina* Weinland, 1858, *Tænia capensis* Moq.-Tandon, 1860, *Tænia lophosoma* Cobbold, 1866, *Tænia fenestrata* Huber, 1896, *Tænia hominis* v. Linstow, 1902, etc., etc.

Historical and Geographical Data.—*Tænia saginata* was probably the worm for which the Egyptians of the Middle Kingdom prescribed a decoction of pomegranate bark. It was one of the common helminths of ancient Greece and was almost universally present in Europe from the Middle Ages until the rediscovery of the Greek prescription of male fern for its expulsion (i. e., Madame Nouffer's "Celebrated Remedy"). The larval stage (cysticercus) was apparently first observed in beef muscle by Wepfer in 1675, and in 1861 Leuckart (1862) first demonstrated that cattle are the intermediate hosts and the source of human infection.

This worm has a comopolitan distribution wherever beef is eaten, but is particularly prevalent in Mohammedan communities. It has a considerably higher incidence than *T. solium*. Likewise, Ethiopians to the present day, just as they did centuries ago, are confirmed raw-beef eaters and boast of the number of beef tapeworms which they harbor. *T. saginata* is widely distributed in Mexico and occurs in about one per cent of the population sampled (Mazzotti, 1944). It is relatively widespread in the United States but its actual incidence is considerably less than that of *Hymenolepis nana*. Stoll's (1947) estimated world incidence is 38.9 million persons, for the most part natives of Africa, the U. S. S. R. and Asia.

Structure of the Adult Worm. *Tænia saginata*, the beef tapeworm, is the principal human representative of the subgenus *Tæniarhynchus*, which contains the unarmed tænid cestodes. The adult worm is an exclusive parasite of man. It lies in the middle length of the small intestine with its head imbedded in the mucosa. Rare cases of its migration out of its normal habitat into the pancreatic duct and into the abdominal cavity are

on record. The adult worm is much larger than that of *T. solium*, due not only to the fact that the proglottids are longer, but also to the greater number of proglottids. Under favorable conditions it may attain a length of 25 meters but it usually averages *not more than 5 to 10 meters and* consists of about 1000 to 2000 proglottids in patients harboring single infections. In multiple infections both the size of the worms and the number of each worm's proglottids are proportionately reduced (Sommer, 1874; Leuckart, 1886; Palais, 1937).

The scolex of *T. saginata* (Fig. 164) is quadrate-obovate in shape, measures 1.5 to 2 mm. in diameter, and is characterized by having four symmetrically arranged, hemispherical, suctorial pockets of 0.7 to 0 8 mm.

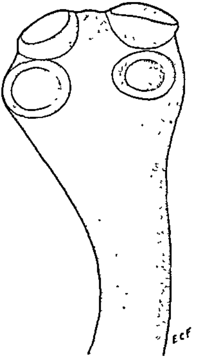


Fig 1

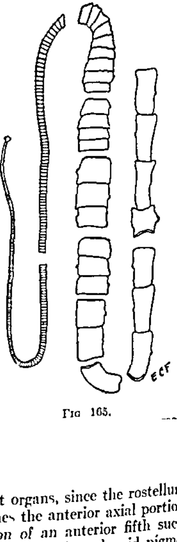


Fig 165.

Fig 164 —Head of T

courtesy of Professor S

Fig 165 —Strobila of

des Menschen)

diameter, which alone serve as attachment organs, since the rostellum is
lacking and there are no hooklets. At times the anterior axial portion is
even sunken, so as to give the impression of an anterior fifth sucker.
Frequently the head is covered with a characteristic melanoid pigment.
The neck (Fig. 165) is about one-half as broad as the head and several
times its length Behind this region there are several centimeters of very
immature proglottids, in which the reproductive organs have not yet
developed. The proglottids gradually increase in size, reaching a maximum
width of about 12 mm These proglottids are still broader than long. The
mature proglottids (*i. e.*, those containing fully-developed reproductive

organs but with the uterus still in the form of an elongate sac) are usually found near the middle of the strobila. They are somewhat broader than long (Fig. 166). Multiple testes, numbering 300 to 400, are distributed throughout the proglottid on the dorsal half, but they are most abundant in the lateral fields. Vasa efferentia from the testes assemble in dendritic fashion towards the center of the proglottid, joining to form the pouch-like seminal vesicle, which, in turn, empties into the vas deferens, a tightly twisted tubule which proceeds directly towards the lateral margin, there to enter the cirrus pouch, which contains the muscular cirral organ. This, in turn, opens into the genital atrium

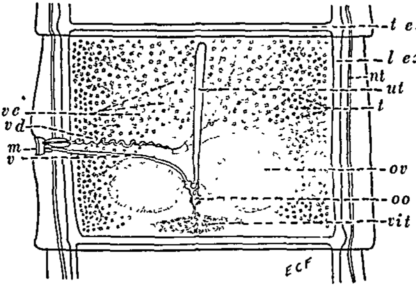


FIG 166 – Proglottid of *Tænia saginata* showing important organs *l exc* lateral excretory trunk, *m*, ♂ pore or genital atrium *nt* lateral nerve trunk *oo* oötype *ov*, ovary *t*, testes *t exc*, transverse excretory canal *ut* uterus *v*, vagina *vd* vas deferens *ve* vasa efferentia, *vit*, vitellaria × 10 (Original)

Just below the vas deferens is the rectilinear vagina, with its outer extremity opening into the genital atrium and its inner opening into the anterior face of the ootype. The ovary consists of two distinct lateral branches, with an intermediate transverse collecting sinus, from which a small oviduct proceeds posteriad, joining the vagina just before the latter opens into the ootype. The vitellaria consist of a compact ellipsoidal gland, situated in a transverse position immediately behind the ootype and having a short duct leading into the latter The ootype is surrounded by a minute, spherical cluster of "shell glands" The uterus in the mature proglottids is a narrow tubular pocket, arising from the antero-ventral face of the ootype and ending blindly near the anterior margin of the proglottid

The process of egg manufacture begins after the proglottids have matured After the eggs are assembled in the ootype they are shoved into the uterus, which becomes more and more distended and which soon begins to develop the characteristic lateral arms When the proglottids become so gravid with eggs that the uterus assumes the characteristically branched

appearance (Fig. 132, *1*), such as obtains in the terminal fifth of the worm, the generative organs atrophy and the proglottids become mere storage-houses for the eggs. The proglottids then separate, usually one at a time, from the parent worm and for a time

Due to abrasion or to disintegration

uteri burst longitudinally along the

migrate out of the gut or are evacuated in the feces.

The Life Cycle of the W

already fully developed.

a mother embryonic memb

On extrusion from the uterus this outer membrane is soon lost, so that the egg commonly recovered from the feces has a shell composed of many truncated pyramids and the hexacanth embryo within (Fig. 167). These eggs measure 31 to 43 μ in diameter and number about 80,000 for each average proglottid (Penfold, Penfold and Phillips, 1937). The eggs in gravid segments, as well as those set free, are capable of immediate development within the ox. After introduction into the duodenum or jejunum of this, the usual intermediate host, the shell is digested off, and the hexacanth embryo is set free, whereupon it penetrates through the gut wall into the blood vessels or lymphatics, settling down in skeletal muscles, commonly the pterygoid and tenderloin, and in the wall of the heart, where it develops in sixty to seventy-five days into the mature bladderworm or *Cysticercus bovis* (Fig. 168).

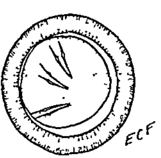


FIG 167.—Egg of *Tænia saginata.* × 666 (Original)

This larva is an ovoid, milky-white object, frequently possessing an opalescent translucency, and measuring 7.5 to 10 mm. in breadth by 4 to 6 mm. in length. Within the bladder is an invaginated head which possesses in miniature the characteristics of the adult scolex.

Apparently kids and sheep have been experimentally infected with *Tænia saginata* eggs. The buffalo, giraffe and llama are recorded as natural hosts. Cases of cysticercosis bovis in man have been reported but all of the diagnoses are open to question except that of Fontan (1919), who described *Cysticercus bovis* from the mammary gland of a patient also harboring the adult worm, and that reported by De Rivas (1937), from an autopsy in which cysts of *Tænia* without rostellar hooklets were recovered from the following muscles: semitendinosus, gluteus maximus, semimembranosus, rectus and pyramidalis.

Epidemiology.—*Tænia saginata* is the most common human tapeworm. Its incidence is several fold higher than that of *T solium* in France, Switzerland, Denmark, Italy and the United States In Mohammedan countries it is common, while *T. solium* is practically unknown. In the Far East it is by far the more prevalent species.

Human infection is acquired from the consumption of raw or rare beef containing the cysticercus larvæ of this worm. Cattle acquire the infection from grazing on ground polluted by human feces containing the eggs of the parasite. Pastures polluted by sewage from urban areas are a special

source of infection for the intermediate host. Under suitable conditions of moisture and mild temperature the eggs may remain viable on pastures for eight weeks or more (Penfold, Penfold and Phillips, 1937) In 1912 in the United States, Federal inspected cattle had a 0.14 per cent infection; in 1930 and since that time 0.37 per cent have been found infected. In Bulgaria the infection in cattle varies between 0.07 and 0.16 per cent, in water buffaloes it is negligible.

Pathogenesis, Pathology and Symptomatology.—The adult *Tænia saginata* produces a clinical picture similar to *T. solium.* Towards the end of the incubation period diarrhea and hunger pains frequently develop and a loss of weight may occur. In children there is a characteristic increase in ... Rarely ... complete ... py instituted in time, death may ensue (Hurst and Robb-Smith, 194-). A moderate leukocytosis may be present during this period but later a leukopenia may be discovered. An eosinophilia of 6 to 34 per cent has been reported.

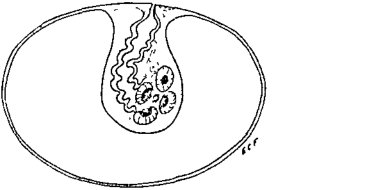


FIG. 168.—*Cysticercus bovis*, with scolex invaginated into bladder. (Greatly enlarged). (Original.)

Cases are on record in which the proglottids of this worm have become lodged in the appendix and have produced appendiceal colic. In one instance specific chemotherapy was instituted, followed by complete recovery from the "acute appendix."

Diagnosis.—This is based on the recovery of gravid proglottids with lateral uterine arms numbering more than fifteen (usually 18 or more) (Fig. 132, *1*) as contrasted with the smaller number in *T. solium* (7 to 13, usually 9). It is impossible to differentiate the eggs of this species from those of *T. solium*. At times the proglottids evacuated in the feces of the patient have partially disintegrated or have lost their distinctive characters. Administration of a saline purge will usually result in the discharge of more proximal proglottids which can easily be identified.

Therapeusis.—*Oleoresin of Aspidium*, as indicated for *Diphyllobothrium latum*, *extract of Aspidium* and *carbon tetrachloride*, as recommended for hookworm infection, are the anthelmintics of choice. Espersen (1946), in Denmark, has reported on the use of the extract of Aspidium in 191 cases of tapeworm infection (179 *T. saginata*, 3 *T. solium* and 9 *Diphyllobothrium*

latum). Employing a maximum dosage of 10 Gm. or 0.67 Gm. per year of age for children, he succeeded in evacuating the scolex in 72 per cent of the patients. Occasionally there was palpitation, tachycardia, a feeling of cardiac depression, jaundice, and in women accelerated menstrual bleeding. In addition, there are the following available alternative anthelmintics which are at times successful in evacuating these worms: pelletierin tannate and other preparations of pomergranate bark (*Punica granatum*); tetrachlorethylene, as administered in hookworm infection; the strained infusion of mashed pumpkin seed; decoction of areca or betel nut; infusion of quassia wood; hexylresorcinol crystoids, and oil of chenopodium. (For a consideration of these tæniafuges or tæniacidal preparations the reader is referred to pp. 642, 646, 656, 662.)

It is essential that the patient be given adequate pre-treatment preparation, that the anthelmintic be fresh, properly prepared and administered according to recommendations, and that the bowels be adequately evacuated by saline purgation within a few hours after specific medication. The stools passed for several hours after treatment should be carefully searched for the scolex of the worm. Failure to find the "head" is almost presumptive evidence that the treatment has been unsuccessful and that a new strobila will develop.

In addition to the time-tested tæniafuges and tæniacides two drugs previously employed for other parasitic infections have proved of considerable value in eradicating *Tænia saginata*. In 1947 Neghme and Faiguenbaum reported on the use of *atabrine* for the removal of *T. saginata*, *T. solium* and *Hymenolepis nana*, with cures in 25 of 30 patients treated. More recently Pipkin and Rizk (1949) have tested this drug in 42 school children in Lebanon, aged 4 to 19 years, who were infected with *T. saginata*. Employing a total dosage of 0.5 to 1.0 Gm., depending on age and weight, administered in two doses an hour apart and followed in three hours with a purge, only 7 of the group were demonstrated to be freed of the infection. Because of toxic manifestations in these patients the drug was discontinued as an anthelmintic. Brown (1948) and Hernández-Morales and Santiago-Stevenson (1949) have reported on the efficiency of hexylresorcinol administered transduodenally as an emulsion. These workers state that it is very effective against *Tænia saginata*, whereas only moderate success has attended its administration orally in hard gelatine capsules (*i. e.*, crystoids anthelmintic).

Prognosis.—Usually good. Complete eradication of the worm requires the evacuation of the "head" as well as the remainder of the worm, since an attached "head" will produce another complete worm of several meters length in three to six months' time.

Control.—All beef consumed by man should be carefully inspected for cysticerci. In the United States only about two-thirds of the cattle, exclusive of calves, is inspected by the Federal Government (*Hall, 1935*). Cattle which have not been exposed to infection for a year or more are usually safe for consumption, since any previously acqured cysticerci will have calcified or caseated during that time. Thorough cooking of beef insures complete safety. The practice of prescribing raw or rare beef for persons suffering from anemia, tuberculosis etc., and for pregnant women.

has been responsible for infection in no small number of persons. Some alternative therapeutic, as liver or iron, should be prescribed as a safeguard against this infection.

In order to exterminate tæniasis saginata from a lightly endemic area, cattle should not be allowed to graze near ground polluted with human night-soil. On the other hand, Penfold and Penfold (1937) have found that calves readily develop an immunity when pastured on heavily infected sewage farms, so that after two years they are essentially innocuous.

Tænia confusa Ward, 1896. (The confused tapeworm.)

Synonym.—*Tænia bremneri* Stephens, 1909.

This species of *Tænia*, of the subgenus *Tæniarhynchus*, has been previously recorded four times from man in the United States, twice from Nebraska, once from Texas, and once from a Louisiana patient. The author has also diagnosed one additional case each from Illinois, Tennessee and Mississippi. An incomplete specimen of *Tænia* which came from a woman in Northern Nigeria and has been

FIG. 169.—Head of *Tænia confusa*. × 21. (Original.)

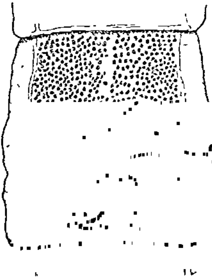


FIG. 170. Mature proglottid of *Tænia confusa*. × 4. (After Chandler, Journal of Parasitology.)

described by Stephens as *T. bremneri*, is probably referable to *T. confusa*. Briscoe (1929) has found 3 cases of *Tænia* which he diagnosed as *T. confusa* in 528 in-patients in East Africa. Iwata (1939) reports this species from Japan. The worm has not been recorded from other hosts and its life history is incompletely known.

The entire worm measures from 5 to 8 meters in length and consists of from 700 to 800 proglottids. The majority of these are longer than broad and the terminal ones are unusually long and narrow (Fig. 132, *4*). The head, which is unarmed (Fig. 169), is dome-shaped and measures about 1.5 to 1.0 mm. It possesses four very muscular suckers, is unarmed, and is sharply set off from the neck region. The proglottids do not have the sexual organs fully developed (Fig. 170) until they are approximately squarish (9 by 9 mm.). The terminal (*i. e.*, gravid) proglottids measure from 25 to 34 mm. in length by 3.5 to 9 mm. in width. The genital pore is

characterized by having a plug-like papilla which nearly fills the atrium. Both cirrus pouch and vagina open at the tip of the plug. The gravid uterus is distinquished by the great irregularity of the divisions of the lateral arms, which are deeply constricted near their origins but are swollen towards their blind ends. The uterine eggs measure 33 by 42 μ and possess distinct polar filaments like those of *T. saginata*.

Calves were found by the author to be an acceptable intermediate host of *T. confusa*. The cysticerci mature in about twelve weeks (Faust, 1930).

The clinical aspects of this infection have not been carefully studied, although the author's case suffered from abdominal discomfort. Administration of the *oleoresin of Aspidium* resulted in removal of the entire worm with its head.

Tænia africana v. Linstow, 1900. (The African tapeworm.)

Two specimens of this species of tæniarhynchid cestode were obtained by Fulleborn from a native soldier in the vicinity of Nyasa Lake, East Africa. The speci- ... broader than long

gravid ones measuring about 7 mm. in length by 12 to 15 mm in breadth The genital pores alternate regularly in the mid-lateral line. The cirrus pouch is pyriform and thick-walled and both cirral organ and vagina are beset with ciliary bristles. The vas deferens is highly convoluted. The testes are very numerous and occupy the greater portion of the mesenchyma. The large bilobed ovary consists of ... gland

consists of a median longitudinal tube with unbranched lateral arms radiating from it. The life history and clinical aspects of this infection are undescribed.

Tænia tæniæformis (Batsch, 1786) Wolffhügel, 1911.

Synonym.—*Tænia infantis* Bacigalupo, 1922.

This worm is a normal parasite in the intestine of cats, which become infected from consuming raw rat flesh. A single human case has been recorded, that of a five-year-old child in Buenos Aires, Argentina.

Genus Multiceps Goeze, 1782

(genus from *multus*, many, and *caput*, head)

Multiceps multiceps (Leske, 1780) Hall, 1910. (The "gid" tapeworm, causing cerebral cœnuriasis.)

Synonyms.—*Tænia multiceps* Leske, 1780; *Vermis vesicularis socialis* Bloch, 1780; *Tænia vesicularis cerebrina* Goeze, ... Batsch 1786, ... 808, *Polycephalus ovinus* Zeder, 1803, *Cœnur* ... *Tænia cœnurus* Kuchenmeister, 1854; *Multiceps gaigeri* ...

Biological, Morphological and Epidemiological Data.—The adult stage of this tæniid cestode, like that of *Tænia solium*, is characterized by having an armature of ... plete worm measures 40 to 60 cm in ... ble

150 to 170 μ and the smallest ones 90 to 130 μ. ... 8 to 10 mm. and a breadth of 3 to 4 mm. The gravid uterus consists of a med...

long median stem or l

ns on either side The eggs
n the small intestine of the
the parasite, although the
wolf may also serve in this capacity.

The life history of *Multiceps multiceps* was first demonstrated by Kuchenmeister in 1853 The gravid proglottids or the liberated embryonated eggs are passed in the dog's feces If the eggs are washed into puddles from which sheep or other grazing animals drink, or
digestive tract of
embryo escapes
vessels or lymph channels. Upon coming to a place of lodgment it may proceed to develop or it may begin an active migration for a while Usually only those embryos which reach the brain or spinal cord are able to effect complete development, although Sopikof (1931) has found the larva of this species localized in the muscle of

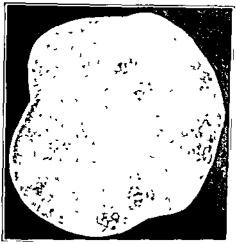


FIG. 171.—*Cœnurus cerebralis* Cyst from brain of sheep × ½ (After Hall, U S Department of Agriculture)

sheep. Once arrived in this location, the embryo becomes transformed into a *cœnurus*, a type of bladderworm (Figs 171, 172) which differs from a cysticercus in having multiple heads invaginated from the wall into the bladder cavity As many as 100 of these scolices may develop within a single cœnurus Each scolex (Fig 172 *B*) is a miniature replica of the head of the adult worm and, under, favorable conditions, is capable of producing a complete worm. Ordinarily such opportunity is afforded when sheep- or cattle-dogs consume the brains of animals that have died of the bladderworm infection. The common larval hosts are sheep and goats, chamoix, cattle, horses, gazelles, antelopes and other herbivores, as well as the simians, *Macaca mulatta* and *M. silenus*, have also been recorded as intermediate hosts

The first authentic human case was a Paris locksmith, obtained in 1911 and reported by Brumpt, 1913 with a history of aphasia and epilepsy. *Postmortem* search revealed the presence of a degenerate cœnurus (with free hooklets, a complete scolex and numerous calcic granules) in a lateral ventricle of the brain, while imbedded in the substance of the cerebrum was a complete cœnurus with no less than 75 scolices It was inferred that the infection had resulted from contamination with eggs of the adult worm in dog's feces.

A second human infection with the cœnurus of *M. multiceps* was reported by Culver (1941); at autopsy of a South African native cysts of this species were found

"unattached and floating in the left ventricle of the brain." Also in 1941 Clapham published the record of cerebral cœnuriasis in a thirty-nine-year-old British sailor, *from whom at autopsy a fully-developed cœnurus of M. multiceps* was recovered from the posterior horn of the lateral ventricle. *A fourth case, possibly due to M. multiceps*, was that of a fourteen-year-old girl who developed paraplegia in December, 1946. A cœnurus was removed from the spinal cord. The girl had never been outside Great Britain but may have contracted the infection in Wales between 1943 and 1945 (Buckley, 1947).

Pathogenesis, Pathology and Symptomatology.—The adult stage of *Multiceps multiceps* in the dog's intestine gives rise to no particularly significant symptoms. The cœnurus in intermediate hosts produces "gid" or vertigo, due to the growth of the cœnurus in the brain and spinal cord. The first reported human case developed aphasia, alexia, inability to write or calculate, and frequent epileptiform seizures. These symptoms were attributed to an intracerebral parasite, the diagnosis having been later confirmed by autopsy.

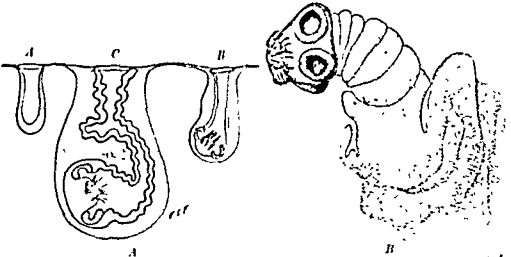


FIG. 172. *Cœnurus cerebralis.* *A*, three successive stages, *A*, *B*, *C*, in the development of the cœnurus scolex (original). *B*, head dissected from wall of cœnurus, greatly enlarged. (After Hall. U. S. Department of Agriculture.)

Diagnosis. This can be made only tentatively during life and *requires post-mortem* confirmation. The parasite must be differentiated from the more frequent *Cysticercus cellulosæ* and hydatid cysts of the brain, cœnuri of other species of *Multiceps*, brain tumors and other cerebral lesions.

Prognosis. Grave.

Therapeusis. No treatment is possible except symptomatic care of the patient. Surgical removal appears to be impractical.

Control. Extreme care should be exercised in infected areas *to prevent* contamination from dog's feces. When epidemics in sheep or other reservoir hosts break out, the carcasses should be burned to prevent infection on a large scale in dogs, accompanied by periodic administration of kamala or other satisfactory anthelmintics to exposed dogs.

Multiceps glomeratus Railliet and Henry, 1915.

Synonyms.—*Cœnurus glomeratus* (Railliet and Henry, 1915) Turner and Leiper, 1919; T... (Railliet and Henry, 1915) Brumpt, 1922 ... stage which

from the intercostal muscle of a native of Northern Nigeria A second case was referred to this species by Taramelli and Dubois (1931) The material was obtained from the subcutaneous tissue of the right forearm of a native woman at Pinga, in the

μ long) and 16 small (65 to 70 μ long). It is believed that the human infection was accidental, due to contamination with feces of some carnivore, possibly a dog, which harbored the definitive stage. In the second instance the cyst was described as

[illegible] ts on the [illegible] booklets [illegible] e believes

that the larva obtained from the second patient should not be assigned to *M glomeratus* and that it does not conform to any described species of the genus

A third case of cœnuriasis possibly referable to this species was reported by Cannon (1942) from a thirty-year-old male Nigerian from the same locality from which Turner and Leiper obtained their cœnurus

Multiceps serialis (Gervais, 1845) Stiles and Stevenson, 1905

Synonyms.—*Cœnurus serialis* Gervais, 1845, *Tænia serialis* (Gervais, 1845) Baillet, 1863.

The adult *Multiceps serialis* is a parasite in the intestinal tract of the dog, the wolf and the fox The larva, or *cœnurus* stage, develops in the intramuscular connective tissue of several rodents, as the rabbit, coypu and squirrel, as well as of the baboon and mandril.

Nagaty and Ezzat (1946) report that the cœnurus of this species is about the size of a pigeon's egg or smaller, that the scolices are irregularly scattered along the inner germinal membrane of the cyst wall, that the total number of hooklets on each scolex is 30 to 32, that the larger hooklets measure 148 to 153 microns and smaller hooklets, 94 to 104 microns

The first human infection to be reported was that of a French woman of fifty-nine years, who had never left France and was very fond of dogs In 1933 a palpable tumor mass of oval contour, measuring 90 by 35 mm , was removed from the patient's right buttock. Within the tumor there was a cœnurus with numerous scolices, some of which were fed to a dog Twelve days later, when the animal was sacrificed [illegible] The scolices of th[illegible] diag[illegible]

woman was reported by Brumpt, Duvoir and Sainton (1934) to have three subcutaneous tumors, which were removed by biopsy and at autopsy. Each tumor contained a cœnurus of *M. serialis* One additional cœnurus, tentatively assigned to this species, was obtained at autopsy from the brain of a boy from rural California (Dr Herbert Johnstone, in Craig and Faust, 1943.)

GENUS ECHINOCOCCUS RUDOLPHI, 1801

(genus from ἐχῖνος, spine, and κόκκος, berry)

The genus *Echinococcus* includes typical tænioid worms of minute size, usually not over a centimeter in length, consisting of a head and 3, 4 or 5 proglottids, of which 1 is immature, 1 or 2 are mature, and only 1 or 2 (the terminal proglottids) are gravid The head is crowned with a double row of hooklets The genital pores alternate irregularly in the mid-lateral margins The definitive hosts of members of

this genus are canines and felines, while practically any mammal may serve as the intermediate host. In addition [illegible] *granulosus*, the following specie[illegible] from *Felis concolor* and *F. ya*[illegible] *lupus*; *E. longimanubrius* Cameron, 1926 from *Lycaon capensis*; *E. cameroni* Ortlepp, 1934 from *Vulpes vulpes*, and *E. lycaontis* Ortlepp, 1934 from the hunting dog, *Lycaon pictus*. It appears likely that *Echinococcus cruzi* Brumpt and Joyeux, 1924, obtained in the larval stage from the agouti from Brazil, is the hydatid form of *E. oligarthrus*. It is altogether possible that in South Africa and elsewhere, where species of *Echinococcus* other than *E. granulosus* occur, hydatid cyst in man and domestic mammals may be due to infection with oncospheres of the other species

Echinococcus granulosus (Batsch, 1786) Rudolphi, 1805. (*The hydatid tape worm, causing echinococcosis or hydatid cyst.*)

Synonyms. *Tænia visceralis socialis granulosus* Goeze, 1872; *Hydatigena* [illegible] *echinococcus* [illegible]

185[illegible]
cus [illegible]
Leu[illegible]
1891.

[illegible] hydatid disease, was clinically well known [illegible] lmud makes reference to this condition [illegible] B.C.), Aretæus (9–79 A D), and Galen [illegible] disease. However, the term "hydatid" was used by many of the ancient and medieval physicians for any tumor or swelling of a cystic character. Redi (1684), Hartmann (1685) and Tyson (1691) were apparently the first investigators to suspect the animal nature of the true hydatid cyst. Pallas (1766) suggested the similarity, if not identity, of the human hydatid with that of other animals Goeze (1782) studied the heads developing from the cyst wall, recognized them as tænioid cestodes, and differentiated them from both the cysticercus and cœnurus types of larvæ The adult worms in the intestine of the dog were probably first discovered by J. J. Hartmann (1695), and later by Rudolphi (1808) who believed them to be young forms of *Dipylidium caninum* Van Beneden (1850) recognized them as a separate species (*T nana* v. Beneden, 1858).

The first experiments to determine [illegible] cattle were conducted by v. Siebold (1852), [illegible] recovered large numbers of little tapeworms from the [illegible] confirmed by Haubner, Leuckart, Küchenmeister and Nettleship. The first experiments in which echinococci derived from man were fed to dogs (Kuchenmeister, [illegible] although Naunyn in Germany (1863), [illegible] ustralia bred the adult [illegible] Dévé in France, Dew, [illegible] many other workers in endemic foci throughout the world have continued [illegible] th the biological and clinical aspects of the disease

Geographical Distribution of Echinococcus Granulosus Infection.—*Echinococcus granulosus* is described as cosmopolitan in its distribution, but this statement requires qualification. Considering the distribution of the larval stage in both man and domestic animals, it is found that its known distribu-

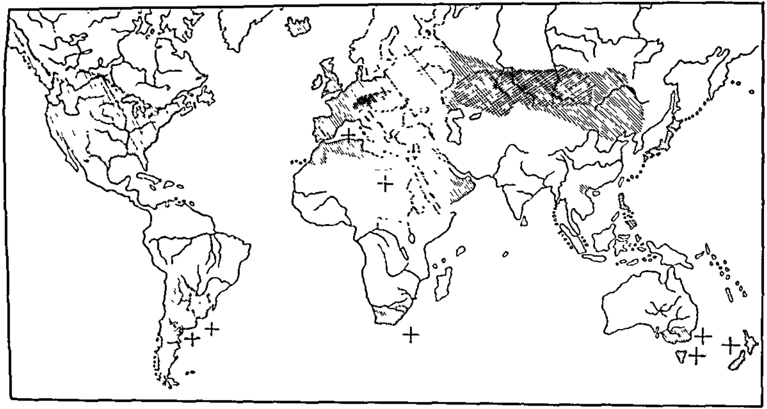


Fig. 173.—Map showing the distribution of *Echinococcus granulosus* in man and reservoir hosts. + indicates heavy centers of human infection. The cross-hatching in Europe and the U.S.S.R. shows areas of human alveolar hydatid disease. (Modified from Faust in Nelson's Loose-Leaf Medicine.)

tion is roughly that of the sheep-, and cattle-raising regions of the world (Fig. 173). Autochthonous human cases are, however, more limited in their distribution, the areas of present-day heavy infection being confined to South Australia (including Tasmania), New Zealand, Cape Colony (S. Africa), Tanganyika (E. Africa), Argentina, Uruguay and Paraguay, southern Brazil, especially the state of Rio Grande do Sul (Pinto and de

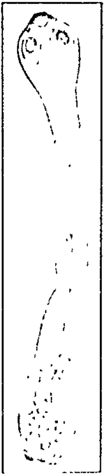


FIG. 174.

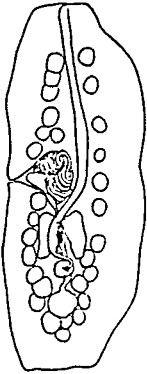


FIG. 175.

FIG. 176.

FIG. 174. *Echinococcus granulosus.* Entire strobila. × 40. (Original photograph from infected Peking dog.)
FIG. 175. *Echinococcus granulosus.* Mature proglottid, greatly enlarged. (After von Erlanger, in Hall.)
FIG. 176. Egg of *Echinococcus granulosus.* × 666. (Original.)

Almeida, 1946), Palestine, Egypt and Algeria. The infection in man is quite general in Central and Northern Europe, although the incidence is not heavy. Similarly, cases of unmistakable local origin are found in Northern China and Mongolia, Japan, Tonkin, the Philippines, Siberia, Arabia, the Punjab region of India, and occasionally the United States. In West China there is a 2.5 per cent infection in dogs but no study has been made of autochthonous human infection (Kuo and Kiang, 1943).

In 1900 about 33 per cent of autopsies in Iceland provided evidence of hydatid cyst. By 1913 the incidence had decreased to 16.6 per cent. Between 1930 and 1944 only about 5 per cent of 1,231 postmortems at Reykjavik showed infection and this was mostly in the higher age groups (Dungal, 1946).

The first human infection with hydatid cyst in the United States was diagnosed in 1808. Through 1940 there was a total of 519 reported cases, 95 per cent in immigrants. Altogether 15 instances of the infection have been diagnosed in the Charity Hospital, New Orleans, Louisiana. Ten of these, including 4 negroes, were natives of Louisiana (Swartzwelder, 1947)

The Adult Worm.—The adult *Echinococcus granulosus* (Fig. 174) is a minute cestode measuring from 3 to 6 mm. in length. The head is pyriform and has a transverse diameter not over 300 μ The anteriorly situated rostellum is armed with a double crown of 28 to 50 hooklets (usually 30 to 36). The four ovoidal suckers measure about 130 μ in diameter The neck is attenuated posterior to the suckers, so that the most constricted region is just in front of the first proglottid, which is immature and is usually somewhat longer than broad. The second one is nearly twice as long as the first and contains a full complement of genital organs (Fig. 175). The third (usually the terminal) proglottid is gravid, it is much broader than the second and may attain a length of 2 mm. In the gravid proglottids the main stem of the uterus develops lateral evaginations, so that its appearance is that of a loosely twisted coil. When the uterine wall becomes fully distended, it bursts open, allowing the discharge of the eggs This may take place before or after the proglottid has become separated from the worm.

Development of the Hydatid.—Most of the present-day knowledge on the hydatid stage of *Echinococcus* has resulted from the studies of Dévé and of Dew. The egg (Fig. 176), which is evacuated in the dog's stool, is so similar to that of other tænioid eggs, including those from species of *Tænia* and *Multiceps* which live as adults in the intestine of dogs, that it cannot be distinguished from them. It possesses a thick, brown shell, composed of many truncated pyramidal parts cemented together (the outer embryonic membrane having been digested off in the dog's intestine), within which is the hexacanth embryo, characterized by three pairs of hooklets.

Unilocular Hydatid.—The egg, upon being swallowed by man or other intermediate hosts as a contamination, passes into the duodenum, where the shell is digested away and the oncosphere, by means of its hooklets, proceeds to invade the mucosa. Barnett (1945) states that the median pair of hooklets is used to enter the tissues and the two lateral pairs are propulsive in function. The embryo works its way through the intestinal wall until it reaches a capillary or mesenteric venule, whereupon it is carried passively in the blood stream until it lodges in some capillary filter. Meanwhile the hooklets have been lost. The first filter is usually in the liver, where the largest proportion of the embryos lodge and become implanted. This accounts for the great preponderance of hydatid cysts of the liver The next filter is in the lungs, where a somewhat smaller number of embryos becomes lodged. Still smaller numbers reach more distant foci and start their development in such localities Thus, within three or four hours after

being swallowed, the embryo may reach the place of its larval development. It is soon attacked by mononuclear leukocytes which probably destroy large numbers of the invaders. The surviving embryos increase rapidly in size, so that by the fourth day they reach a diameter of 40 μ and begin to vacuolate. From three to ten days later a miniature hydatid has been formed, with an inner nucleated germinal layer and an outer hyaline one.

By the end of the third week, when the larva has attained a diameter of ... to show a definite reaction to the parasite. ...ydatid the endothelial cells are arranged ...nfiltration of giant cells and eosinophils. Surrounding this is a zone of fibroblasts, eosinophils and new bloodvessels in process of development. Fibrous tissue surrounds this zone and grades off into normal tissue cells, which may be already undergoing pressure

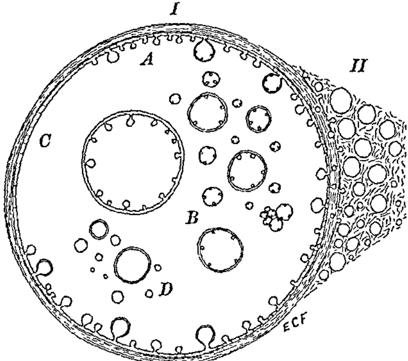
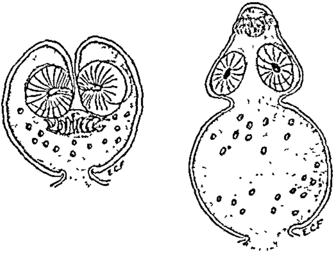


FIG. 177 —Schematic representation of the development of hydatid cyst, daughter cysts, brood capsules and scolices I Endogenous budding (unilocular type). *A*, brood capsule production from germinative layer, *B*, free daughter cysts producing scolices, *C*, sterile germinative layer, *D*, sterile daughter cysts. II Exogenous budding (alveolar type) (Original.)

atrophy, due to the steady increase in size of the hydatid and to the development of adventitious tissue (the *pericyst*). About the fifth month, when the cyst has reached a centimeter in diameter, the outer cuticular layer (the *ectocyst*) has become definitely laminated and essentially devoid of nuclei, while the inner germinal layer (the *endocyst*) is ready to produce brood capsules. These arise from a proliferation of the masses of nucleated cells, which grow and become vacuolated, thus forming minute inner one-layered cysts or vesicles, which ultimately become stalked. Such vesicles or brood capsules develop at many points on the germinal layer (Fig. 177). Due to trauma, the brood capsules frequently become separated from their mother cyst wall and come to lie free in the fluid of the cystic cavity.

Usually these brood capsules develop internal buds, which produce an internal cuticular layer. The cyst wall then forms an invagination, in which the scolex continues its development, becomes stalked, and develops suckers and hooklets (Fig. 178). Meanwhile the scolex has invaginated into its own body in order to protect its hooklets from injury The free brood capsule and free scolices (*i. e.*, "heads") in the cavity of the hydatid cyst are commonly referred to as "*hydatid sand.*" In some cases the hydatid may never produce brood capsules; in other instances these may become sterilized by calcification. Likewise, the brood capsules may fail to produce scolices, in which case they are *acephalocysts.* Again, daughter cysts may be produced by trauma, but their production is not a normal procedure and probably never occurs endogenously. Where they do develop, due to rupture of the primary (mother) cyst wall or to unfavorable



A B

Fig. 178.—Scolex of hydatid cyst. *A*, invaginated in cyst membrane, *B* with evaginated hooklets and suckers × 400 (Original)

environmental conditions for the parasite, they usually become *heterotrophic, i. e.*, they become implanted outside of their original focus of implantation. Such cysts may originate (1) by separation of a portion of the germinal layer from the primary cyst wall, (2) from the cells of the germinative layers of the brood capsule, and (3) directly from scolices The laminated outer layer of the hydatid is sterile and never gives rise either to endogenous or exogenous secondary cysts Dew's explanation of the development of the exogenous cysts is that the process occurs as a herniation of both germinative and cuticular layers of the primary cyst wall through weak regions of the enveloping adventitious host-tissue layers. These herniated portions become separated from the parent cyst and develop independently.

The type of hydatid thus far described (Fig. 179) is usually referred to as *unilocular.* Other varieties are not uncommon. The most frequent abnormal forms are the *alveolar* and the *osseous hydatid.*

Alveolar Hydatid in Man. Ever since Virchow, in 1855, described an alveolar hydatid infection of the human liver, there has been considerable

controversy as to its origin. One school holds that the parasite causing the infection belongs to a different species or, at least, a different variety from that producing the unilocular hydatid. Another group maintains that its form is due to the type of habitat in which the embryo becomes originally implanted, not permitting the development of the unilocular variety. Certain it is that both the structure and character of the alveolar type are markedly different from the unilocular type. It is a malignant, metastasizing tumor, with an irregular, reticulate outline, not definitely delimited from host tissue, as contrasted with the definitely circumscribed, spherical, unilocular variety, usually of a benign character. Structurally (Fig. 180) it is a porous, spongy mass, consisting of multiple hydatid

FIG. 179.—Unilocular hydatid cyst of the human liver, showing scolices attached to the inner (i. e., germinal) membrane of the cyst walls. × ½. (After Faust, in Brennemann's Practice of Pediatrics; courtesy of W. F. Prior Company, photograph, courtesy of H. H. Loucks.)

vesicles, none larger than a pear, frequently sterile or undergoing degeneration or calcification, imbedded in a fibrous stroma. No matter in what tissue it becomes implanted or where its satellites develop, the character and nature of the alveolar type are always the same. There is never free cystic fluid, merely a jelly-like matrix. It tends to grow superficially and to become necrotic in the center, due to elaboration of hydatid toxins. This type is most common in Southern Germany, Switzerland and the Tyrol, Russia and Siberia, but it has also been seen in Iceland, Northern Germany, Italy, France, Uruquay and Argentina. Human alveolar hydatid differs morphologically from the bovine (*multilocular*) type in several important particulars, including the relatively limited character of the latter, without metastasizing elements.

Osseous Hydatid.—This is essentially a simple unilocular cyst which is

not permitted to assume its usually spherical character because of confinement by the dense surrounding osseous tissues. It travels as a naked protoplast along the bony canals, and erodes the osseous tissue with which it comes in contact. Bado (1946) states that the commonest sites of osseous hydatid are the upper ends of the femur, tibia or humerus, the vertebræ and the ribs. The primary focus may be either the diaphysis or the epiphysis. If the lesion originates in the diaphysis, the trabeculæ are destroyed, the bone is thinned and fracture occurs, if it first involves the epiphysis, it becomes hour-glass shaped and proceeds to involve the contiguous bone. (See Fig. 181.) The parasite is usually sterile but may produce scolices and even endogenous daughter cysts in case it reaches open spaces. Osseous hydatid has been experimentally demonstrated in the rabbit (Dévé, 1948; Pérez Fontana, 1948).

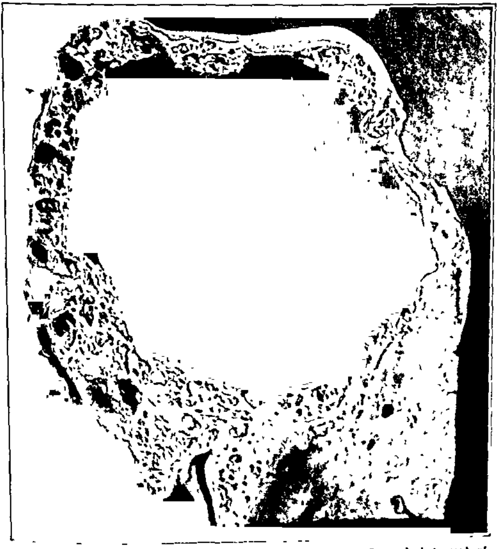


Fig. 180.—Alveolar hydatid cyst of human liver. Natural size. (Original photograph of material from Switzerland.)

Dew has attempted to explain the several varieties or types of hydatid cysts on the basis of the relative development of the four functions of the germinative layer, namely, growth, budding of new reproductive elements, elaboration of hydatid fluid and production of cuticle. In unilocular hydatids all four functions proceed synchronously. In alveolar hydatid the growth function becomes exaggerated, giving rise to metastasizing roots. Thus, this variety is believed to represent a "functional dissociation of the properties of the germinal material."

Epidemiology.—Human infection is always with the larval or hydatid stage of *Echinococcus granulosus* and results from swallowing the eggs of the worm, passed in infected dog's feces and reaching the human mouth from contamination of fingers or from food or drink served in fouled containers or with contaminated utensils. The most common reservoir hosts of the larval (*i. e.*, hydatid) stage are sheep (optimum host), cattle, pigs, horses, camels and goats. The infection in its larval form has also been recorded from monkeys (*Macaca syrichta fascicularis*, *M. mulatta mulatta*, *M. sylvana*, *Papio comatus comatus*), the Asiatic elephant, the argali (*Ovis ammon ammon*), the antelope (*Tetracerus quadricornis*), the zebra, the kangaroo, the mongoose (*Herpestes ichneumon*), the deer, the moose (*Alces alces alces* and *A. alces americanus*), the giraffe, the tapir, the dog, the cat, the leopard, the squirrel and the rabbit. The dog, the wolf, the jackal and the domestic cat are the only proven definitive hosts. The dog and its wild relatives acquire the infection from consuming the offal of the infected intermediate hosts.

Statistics for Iceland in the past showed an incidence of from 16 6 to 33 per cent infection with hydatid in the human population, and 28 per cent infection with the adult worm in dogs, but in recent years it has been greatly
of hum...
dogs harbor the adult worm, the human population in certain districts is infected with the hydatid up to 2 per cent. In 1000 autopsies performed in the Adelaide (S. Australia) Hospital between 1929 and 1934 there were 26 diagnosed cases o ... (calcified, fibrosed, etc.)
to be that of Upper
51 per cent of the sheep and 4.9 to 12.8 per cent of the pigs are infected ... where 0.07 to 0.08 per cent of the human population suffer from the disease. In Syria and Palestine 70 per cent of the sheep and 40 per cent of the cattle are infected. Condemned carcasses of these animals are consumed by jackals as well as dogs, thus increasing the supply of eggs available for producing the hydatid cysts. In this latter country about 25 per cent of the street dogs are infected. Inthe Punjab, Sami (1938) found 28.8 per ce... of the dogs and nearly 90 per cent of the cattle to harbor hydatids. ... today is
the sheep-raising ...
incidence among some of the peons is reported as high as ... birth-rate (Carbonell and Zwanck) and is increasing faster than the birth-rate (Greenway).

Most hydatids cysts in man are acquired in childhood. This may be

due in part to greater susceptibility but it is undoubtedly associated with infected dogs. Frequently the unilocular cyst may grow for five to twenty years before it is diagnosed. It may be almost as old as its host (Barnett, 1945). Ferro (1946) has found that there is a definite tendency for hydatid cyst to be more common in members of the same family than in the general population.

Brea *et al.* (1945) have reported on 150 cases of pulmonary hydatid cyst operated on in Buenos Aires, Argentina between 1919 and 1943 Of this total, 102 were males; 129 were natives, 11 Spaniards, 7 Italians, one a Jugo-Slav, one a Frenchman and one an Arab. The great majority provided evidence of having acquired the disease in the Province of Buenos Aires. The percentage age distribution was as follows: 1–10, 1 4, 11 20, 20.6; 21–30, 34.0; 31–40, 24.7; 41–50, 11.3; 51–60, 6.0, and 61 and older, 2 0

Pathogenesis, Pathology and Symptomatology of Hydatid Cyst. – The seriousness of hydatid cyst depends on the nature of the tumor, whether unilocular, alveolar, or osseous, and on the organs or tissues in which the echinococcus embryo becomes implanted. If the embryo settles in an optimum habitat, it develops normally into a unilocular cyst, with the proper balance of its functions, resulting in the production of brood capsules, scolices and the elaboration of *hydatid fluid* filling the cystic cavity. According to Lemaire and Ribère (1935), the average hydatid fluid has a specific gravity of 1.0118 and a pH of 6.7, it contains creatinin, inosite, ammoniacal salts, lecithin, and both proteolytic and glycolytic enzymes. Ymaz Apphatie (1937) has found that the albuminoid fraction of hydatid fluid has more potent antigenic properties than the saccharine fraction or the unfractionated fluid.

An inflammatory reaction is set up in the host cells surrounding the cyst, leading to the development of a fibrous tissue adventitia which more or less successfully insulates the parasite from vital host cells Under such conditions the hydatid toxin is localized, as demonstrated by the infiltration of eosinophils in the immediate area around the cyst. Only where seepage of the hydatid toxin occurs through incomplete cuticulization, inclusion of [illegible] does the toxin get into the ge[illegible] be expected. I[illegible] ilocular cyst result in its sterilization or the production of endogenous daughter cysts Rupture of a fertile cyst may result in the dislodgment of germinative tissue and the development of daughter cysts exogenously. If the echinococcus embryo has become implanted into closely confined quarters, such as cannalicula of the bones, it is unable to proceed to typical cyst formation but permeates all available spaces, eroding and weakening the adjacent osseous tissue (Fig. 181). Only in case it escapes from its cramped confines is it able to proceed to normal cyst formation. The tremendous size to which abdominally implanted hydatid cysts frequently develop gives rise to increased discomfort as the cyst grows. In case it is surrounded by distensible host tissue, the latter frequently becomes modified from pressure atrophy. The implantation of echinococcus embryos in the brain or orbit produces grave symptoms in a relatively short time, the increased dysfunction frequently resulting in sudden death.

Barnett (1945) states that primary peritoneal cysts are rare; that primary brain hydatid nearly always occurs in childhood, while *in adults it is* usually secondary to cardiac hydatid.

On the basis of statistics compiled by various workers (Thomas, 1894, in Australia; Peiper, 1903, in Germany; Dévé, 1912, in France; Pinto and

FIG. 181.—Osseus hydatid of the upper right femur in man. Roentgenogram shows the extensive erosion of the bone and involvement of adjacent tissues. (After Faust in *Nelson's Loose-Leaf Medicine*, courtesy of Thomas Nelson & Sons, photograph, courtesy of H. H. Loucks.)

de Almeida in Brazil, Magath, 1921, in North America, and Loucks, 1930, in China), the relative frequency of cysts in the various organs of man is as follows: liver 57–76.6 per cent; lungs, 3.8–14 per cent; omentum, mesentery and peritoneum, 1.37–18.2 per cent; pleura, 0.7–0.9 per cent, skin, subcutaneous tissues and musculature, 0.7–9.1 per cent; spleen, 1.2–9.1 per cent; heart, rare, brain, 0.9–2.0 per cent; spinal cord, 0.8–0.9 per cent; orbit, rare; kidneys, 1.6–6.1 per cent; male pelvis, 0.2 per cent; female

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Fig. 181 ... Roentgenogram shows the ... (After Faust in Nelson's ... Loucks) ... Thomas Nelson & Sons, photograph, courtesy of H H.

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cyst of the liver is summarized as follows: (1) Expose the adventitia surrounding the cyst by incision over the most prominent or most dependent part of the tumor. (2) Thoroughly wall off the exposed surface of the wound. (3) Aspirate the contents through a large-caliber needle or trocar connected with a closed suction apparatus (4) Inject 10 to 30 cc 10 per cent formalin solution and withdraw the fluid in five minutes (5) Incise through the adventitia down to the actual cyst. (6) Separate the cyst from the adventitia and remove the cyst and its contents. (7) Swab the adventitia with 10 per cent formalin, allowing a few cubic centimeters to remain in the site. (8) Obliterate the cavity (capitonnage) by intracapsular sutures wherever possible. (9) Close the adventitia by a double row of catgut sutures. (10) Close the cavity without open drainage anchoring the adventitia to the tissue beneath the line of incision

Surgeons in Uruguay, where the removal of hydatid cyst has provided both experience and skill, employ different technics depending on the

liver, following laparotomy and discovery of the exact location of the lesion, the fluid contents are very rapidly aspirated to prevent spillage into the peritoneal cavity. Following incision into the cyst itself the wall of the cyst is scraped out as well as possible and the remaining parasite tissues treated with one per cent formaldehyde. Then the cavity is washed out with physiological salt solution, leaving no appreciable amount of formaldehyde Finally the cavity is collapsed, its cut edges sutured together and the operating wound closed. If the cyst is in the lungs it is characteristically encapsulated. Entry is made between the ribs, the cyst is completely

parasite and cure of the disease."

Jorge and Re (1946) have proposed biological therapy in hydatid disease. This consists in the intradermal introduction of small amounts of hydatid antigen periodically two or three times a year for a period of years. Together with calcium and ascorbic acid the antigen is stated to cause complete hydrolyzation of the cyst and its biological sterilization.

Prognosis.—Fair in operable cases; grave in inoperable cases Alveolar

Care not to spread the infection during

Recurrence may be anticipated within

: the cases, due to failure to remove all of the parent cyst, or, more frequently, to development of secondary cysts from scolices spilled into the operative cavity. In Australia the registered deaths have constituted 16.6 per cent of the recorded cases of this disease (Barnett, 1936.)

Control.—Infection results from caressing infected dogs and from contact with dirt, vegetables and dishes contaminated with the eggs from infected dog's feces. Thorough washing of hands before eating would materially

ecial attention in endemic areas

ly habits. Dogs should be pre-

and hogs in endemic foci, especi-

SECTION III

THE ACANTHOCEPHALA, OR THORNY-HEADED WORMS

CHAPTER XXI

THE ACANTHOCEPHALA, OR THORNY-HEADED WORMS

INTRODUCTION

This group of exclusively parasitic worms (Fig. 182) is composed of species which are characterized by having two distinct parts to the body, *the proboscis* (*p*) and the *body proper*. They are elongate, unsegmented worms, more or less flattened (*i. e.*, deflated or decompressed) when alive, but turgidly cylindroidal or spindle-shaped when preserved or in a hypotonic medium, and vary in length from a few millimeters to 50 or more centimeters. The proboscis, which is usually retractile into a muscular proboscis sheath (*psh*) and is in most species armed with several rows of recurved hooks, is at the anterior extremity of the worm and serves as an organ of attachment. Beneath the thin cuticula there is a hypodermis which is not separated into cellular units (*i. e.*, it constitutes a syncytium).

Internally one or more pairs of elongate *lemnisci* (*l*), continuations of the subcuticula and enclosed lacunæ, extend posteriad from the region of the

[illegible]

is apparently present in all species. The *nerve mass* (*n*) lies within or on the proboscis sheath.

The two sexes are separate. The genital pore is at the posterior extremity. In the *male* (Fig. 182A) it is surrounded by a campanulate *bursa* (*bu*). Two *testes* (*t*) [illegible] *cle* (*cgr*) and a *suspensory* [illegible] In the *female* (Fig. 182B) [illegible] or end of the sheath to the uterine bell. The *ovary* first breaks up into egg balls or *floating ovaries* from which a large number of eggs develop These *eggs*, which are provided with three (at times probably four) enveloping membranes, lie free in the body [illegible] bryos being removed [illegible] means of a muscular [illegible]

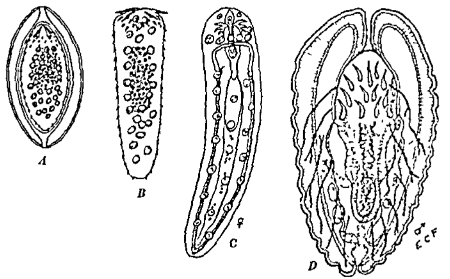
In addition to the fact that the males are much smaller than the females, there are frequently other external characters which distinguish the two sexes, including the shape, the character of proboscis and body spines, and the proboscis-structure.

With the exception of the egg stage the Acanthocephala are parasitic during their entire life cycle, with no free-living phase. The eggs, which are passed in the feces of the vertebrate host, are usually unembryonated and complete their embryonation before they are infective for the inter-

structures become recognizable as those of the adult worm This is the last stage in the arthropod host. On ingestion of the infected arthropod the appropriate vertebrate host acquires the infection, the worm develops to maturity, mates and egg-laying is begun The more important developmental stages are shown in Fig. 183.

CLASSIFICATION OF THE ACANTHOCEPHALA

Since the time of Claus (1890) and Perrier (1893) the Acanthocephala have traditionally been grouped with the Nematoda and Gordiacea in the Nemathelminthes. More and more this allocation has been recognized as an unnatural one and certain students of these groups, especially Van Cleave and Chitwood, have produced evidence demonstrating that this



[illegible] developmental stages of [illegible]

association must be abandoned. Because of the protonephridial excretory system discovered in *Macracanthorhynchus hirudinaceus*, *Gigantorhynchus major* and several other species of the Acanthocephala; because of the loose parenchymatous matrix and lack of a body cavity; because of the presence of hooklets on the embryo (acanthor) hatching from the egg, and because of the more or less flattened appearance of the body, it has been suggested that [illegible] of the flatworms most [illegible] re logical than the [illegible] Nemathelminthes, evidence is not sufficiently convincing to justify their allocation to the Platyhelminthes. There are two other possible courses of action, (1) to elevate the Acanthocephala to the [illegible] rank as a class, without designati[illegible] *sedis incerta*). In conformity with [illegible] phylum rank.

infected; in the United States, *Phyllophaga ferrida*, *Xylorycles satyrus*, *Strategus julianus*, *Phyllophaga rugosa*, *P. fusca* and *P. vehemens* have been found to be suitable intermediate hosts; in Argentina, *Diloboderus abderus* (Sturm), *Phanæus splendidulus* (Fabr.) and *Gromphas lacordairei* Brull have been successfully infected by Wölffhügel. On ingestion of these infected larval beetles the mammalian host becomes infected.

Fig. 185.—Photomicrograph of partially embryonated egg of *Macracanthorhynchus hirudinaceus* × 500 (Original.)

Epidemiology and Clinical Data.—The worm is practically cosmopolitan in distribution. The pig, the wild boar, the peccary and occasionally dogs and monkeys are the natural definitive hosts. Human cases have been reported by Leuckart (1876), a single immature female found in the intestine of a young boy of Prague in 1857, and designated "*Echinorhynchus hominis*," by Lambl (1859, *Echinorhynchus* from man), and by Lindemann (1865), the latter authority stating that the infection is common among the inhabitants of the Volga Valley in Southern Russia, where Schneider has found that *Melolontha* is eaten raw. However, these reports have not been confirmed and it is uncertain if human infection actually occurs.

In porcine hosts the attachment of the proboscis to the intestinal wall causes a localized area of inflammation, with infiltration of large numbers [illegible]

Genus Moniliformis Travassos, 1915

(genus from *monile*, chain, and *forma*, form)

Moniliformis moniliformis (Bremser, 1811) Travassos, 1915. (The moniliform worm.)

Synonyms.—*Echinorhynchus moniliformis* Bremser, 1811; *Gigantorhynchus moniliformis* (Bremser, 1811) Railliet, 1893; *Echinorhynchus grassii* Railliet, 1893; *Hormorhynchus moniliformis* (Bremser, 1811) Ward, 1917; *Echinorhynchus cestodiformis* v. Linstow, 1904; *Gigantorhynchus cestodiformis* [illegible] *canis* Porta, 1914; [illegible], 1917.

Biological Data.—The moniliform worm is whitish or creamy-white in color, and somewhat attenuated at both extremities (Fig. 186). The body is superficially made up of a series of bead-like pseudo-segments, which resemble [illegible] The cylindrical proboscis (Fig [illegible] 0.21 mm., [illegible] to eight hooks per row, each hook being continuous [illegible] directed root-process. The males have a length measurement of 4 to 5 cm., and have a posterior campanulate bursa copulatrix, which is visible to the naked eye. Each of the two testes is about 2 mm. long. The females have

a length measurement of 10 to 27 cm. The cement glands are in the posterior extremity of the body and measure about 1.5 mm. in length. The eggs (Fig. 188) are ellipsoidal, measure 85 to 118 by 40 to 52 μ and are provided

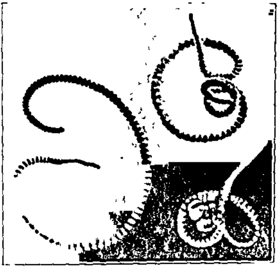


FIG. 186.—Photograph of *Moniliformis moniliformis*. Natural size. (After Travassos, in Revista Vet. e Zoötechnica. 1920.)

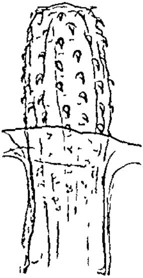


FIG. 187.

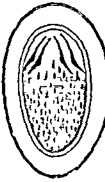


FIG. 188.

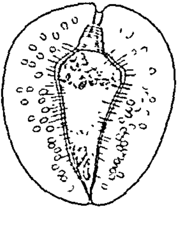


FIG. 189.

FIG. 187.—Proboscis of *Moniliformis moniliformis*. × 100. (After Van Cleave. Proc. Acad. Nat. Sci. Philadelphia.)

FIG. 188.—Egg of *Moniliformis moniliformis* containing embryo (acanthor). × 500. (After Grassi and Calandruccio.)

FIG. 189.—Mature larva (acanthella) of *Moniliformis moniliformis*. Greatly enlarged. (After Travassos, in Revista Vet. e Zoötechnica, 1920.)

with the characteristic three envelopes. The embryos are striated and are covered with spines. The intermediate hosts are species of beetles and cockroaches (*Blaps mucronata*, *B. gigas*, and *Silophilus oryzæ* in Europe

Periplaneta americana in S. America) and possibly other insects. In these hosts the embryos develop into mature ovoidal larvæ enclosed in a cystic capsule (Fig. 189). Infection of the mammalian definitive host results from ingestion of the infected larval host.

In the related but distinct species *Moniliformis dubius*, which parasitizes wild rats in Texas and utilizes *Periplaneta americana* as intermediate host, Moore (1946) has found that eggs ingested by this cockroach hatch in its mid-gut and that the released first-stage larva (acanthor) then slowly penetrates the gut wall, requiring 10 to 12 days to reach the hemocelic cavity of this host. It slowly transforms into the early acanthella stage (thirty-eighth to forty-fourth day) and then matures into the juvenile stage (seven to eight weeks after original entry into the cockroach). Once the murine host has ingested infected cockroaches containing the infective-stage juveniles, five to six weeks ensue before the worms become sexually mature and oviposition begins.

Epidemiology and Clinical Data.—The common hosts of the adult *Moniliformis moniliformis* are rodent species (*Rattus norvegicus*, *R. rattus*, *R. alexandrinus*, *Microtus arvicola*, *Cricetus cricetus*, *Cricetomys gambianus*), the dog [syn. *Echinorhynchus grassii* Railliet, 1893, and *E. canis* Porta, 1914], the cat, etc. Human infections, apparently well authenticated, have been reported from Italy (1 case of natural infection, also 1 of experimental [illegible] nd British Honduras [illegible], have been described [illegible] *13-lineatus*) and from hedgehogs (*Erinaceus europæus*).

The experimental infection of Calandruccio (1888) demonstrated clearly that this species, when present in considerable numbers, produces definite symptoms in man. Nineteen days after ingesting several larvæ, Calandruccio was attacked with severe gastrointestinal pain and diarrhea, accompanied by exhaustion, somnolence and a pronounced ringing of the ears. The period of complete incubation in man (*e. g.*, until eggs of the worm appeared in the feces) was about five weeks. Administration of the *extract of male fern* (*Aspidium filix-mas*) removed all of the worms within three hours, but the symptoms did not disappear for two days following treatment.

SECTION IV

THE NEMATODA, OR TRUE ROUNDWORMS

CHAPTER XXII

THE NEMATODES. STRUCTURE AND LIFE CYCLES

GENERAL CONSIDERATIONS

The **Nematoda** or nematodes are unsegmented roundworms which are usually cylindrical but are more or
posterior ends. They possess a co
Acanthocephala they lack a proboscis
the Nematomorpha (*vide infra*) this cavity is not lined with mesothelium. There are no solenocytes at the inner terminations of the excretory tubules. The gonads are continuous with their ducts. With very few exceptions the sexes are separate. The male is distinguished by being smaller than the female and by usually having the posterior end of its body recurved ventrad. Except in cases where the worm ingests the blood of its host as food, it is usually a creamy or ivory-yellow color. They move primarily by caterpillar up-and-down manipulations of their bodies, but also at times from side to side. The majority of species are at least partially transparent while still alive, but fixation tends to increase their opacity.

A large number of nematode species are parasitic in habits, but probably an even larger number are free-living. Many species are obligatory parasites during a part of their life cycle but have a free-living phase. Forms like *Strongyloides stercoralis* are apparently within certain limits facultatively parasitic or free-living. The host-parasite relationship of the parasitic nematodes has the greatest latitude of any of the helminth groups. Many species are parasitic in or on vegetable tissues, including roots, stems, leaves and even seeds. A wide variety of species are endoparasitic in invertebrate tissues. By far the largest proportion of parasitic nematodes, however, are parasites of vertebrates. Of the 500 genera of nematodes recognized by Baylis and Daubney (1926) 364 are recorded as being parasitic in vertebrate hosts.

STRUCTURE OF THE ADULT ROUNDWORM

The adult nematode varies in size from a filiform object just visible to the naked eye (*Trichinella, Strongyloides*) to a large, rod-like worm (*Dioctophyma*) or an elongate, wire-like worm, which may attain a length of 1½ meters (*Dracunculus*). An extreme alteration from the primitive shape is found in *Heterodera marioni* (a common parasite of vegetable roots), as well as species of *Tetrameres*, the mature females of which become swollen like a lemon. The majority of species are probably under 1 cm. in length. They are primitively bilaterally symmetrical but their parasitic or sessile habits have tended towards the development of radial symmetry.

The somatic layers of the nematode (Fig. 190, A, B, C) consist of (1) a outer integumentary *cuticula*, which is a hardened secretion, probably scleroprotein, derived from the underlyin
an exoskeleton; (2) an epithelial layer or
dermis, just beneath the cuticula, readily
modified in older ones or in large species as to appear to be a syncytia matrix in which fibers and nuclei intermingle; (3) and the *dermomuscula layer*, which constitutes the principal somatic musculature.

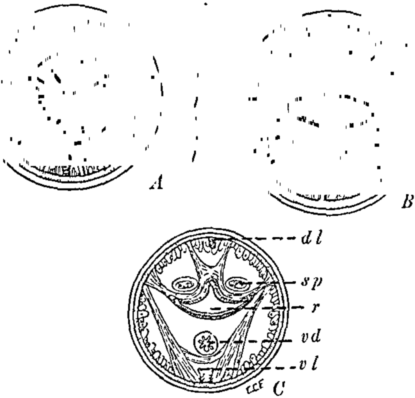


FIG 190 —Transverse section through important regions of *Ascaris lumbricoides*. *A*, at the level of the esophagus (adapted from Goldschmidt, in Zoölogischer Anzeiger). *B*, through the

Arising from the subcuticular layer and projecting out into the body cavity are the four *longitudinal "lines"* (*i. e., cords*), consisting of the dorsal and ventral median "lines" and the pair of lateral "lines" (*Fig. 190*). Cobb (1931) states that "these cords are a basic feature of the nemic anatomy—wellsprings of the cuticle." The muscle bands, which are made up of muscle cells with sarcoplastic processes, consist of one layer of *longitudinal* cells. These cells are divided into four longitudinal groups by the four longitudinal "lines." In its simplest form (*i. e., in Enterobius* and *Ancylostoma*) each of the four units consists typically in cross-section of only two cells and is (
(*i. e.*, they a

on three sides next to the body cavity [Chitwood, 1934, 1937]). In case there are in each group numerous cells, each with its protoplasmic element projecting into the body cavity (*i.e.*, *Ascaris*, Fig. 190 *B*), the type is *polymyarial*. These forms are usually *holomyarial* or *celomyarial* (*i. e.*, the muscle fibers are not only next to the subcuticula but "also extend varying distances up the side of the muscle cell and partially enclose the sarcoplasm" [Chitwood, 1934, 1937]). The muscle elements are non-striated. By synchronous contraction, the muscle bands cause the worm to shorten, unilateral contraction results in bending the worm to one side. There are no circular muscles antagonistic in action to the longitudinals; the elastic property of the cuticle alone serves to elongate the worm. In the **Nematoda**, the group to which all of the true roundworms belong, the body cavity is a *pseudocele*, sometimes referred to as a *schizocele*, *i. e.*, it lacks an epithelial lining such as the **Gordiacea** (Phylum Nematomorpha) possess.

The anterior end of the nematode body is modified for purposes of abrasion (*Esophagostomum*), for attachment to host tissue (*Ancylostoma*, *Gnathostoma*), or for special sensory purposes (*Ascaris*). To these ends teeth, hooks, biting or sawing plates, setæ and sensory papillæ have been developed. Some species, such as *Gnathostoma*, have their cuticle covered with spines, but the majority of species have a glabrous integument. *Bossing is a prominent feature on the cuticle of some of the filarioid* nematodes. Both the anterior and posterior portions of the digestive tract are covered with a continuation of the cuticle. The oral cavity or pharynx is frequently developed into a buccal or pharyngeal pocket or capsule, which may serve as an acetabulum. The alimentary tube consists of three consecutive regions, an esophagus, a mid-gut, and a rectum. The esophagus, embryologically the stomodeum, is a very muscular organ, save in the **Trichinelloidea**, where it consists of a narrow tube, more or less completely surrounded [illegible]

This anterior regio[illegible]

its internal cavity [illegible]

dorsal and two subventral esophageal glands, each with a single nucleus, open into this organ. They have been found to have a lytic function. The esophagus leads posteriorly into the mid-gut, which consists of a single layer of columnar cells (Fig. 190 *B*), lined with non-vibratile cilia, and lacking a cuticular covering. Strong valves, capable of completely closing the lumen, are situated at the junction of the esophagus with the mid-gut. The rectum, embryologically the proctodeum, is short and is lined with cuticle. Anteriorly it is provided with a sphincter muscle. Posteriorly it [illegible] ly anchored to the somatic

[illegible] of two longitudinal tubules imbedded in the substance of the lateral "lines" (Fig. 190 *B*), and primitively opening together into the cloaca. These tubules end blindly posteriad and unite anteriad along the mid-ventral line close behind the mouth, where they open through a single pore. In the more highly modified forms one or both longitudinal tubules may be lacking, with only a lateral or a median gland cell representing the system. The evolution of the excretory system is illustrated in Fig. 191.

Caudal glands, normally three in number and usually situated in tandem in the anterior part of the tail, serve to cement the caudal extremity to objects. They empty through a minute spinneret at the tip of the tail. These glands are common in free-living and non-bursate parasitic species, but are either lacking or highly modified in bursate parasitic forms.

The nervous system (Fig. 192) consists primarily of commissures and longitudinal nerve trunks. The central organ in the system is the circumesophageal ring which completely surrounds the esophagus just in front of the excretory pore. From it there arise six short anterior trunks, innervating the head. The important posterior ventral and dorsal trunks run

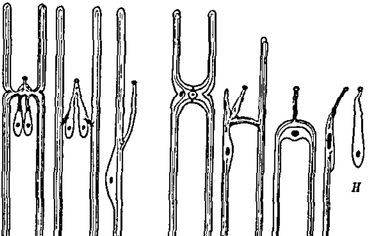


Fig. 191.—Diagrammatic representation of several types of nematode excretory system *A*, rhabditoid, *B*, strongyloid (*Œsophagostomum*), *C*, tylenchoid, *D*, oxyuroid, *E*, ascaroid; *F*, cephaloboid, *G*, anisakid, *H*, chromadorinid (After Chitwood and Chitwood, 1937.)

respectively in the ventral and dorsal median lines of the subcuticular matrix. The four lateral trunks have a double origin. The more dorsal pair arises from the circumesophageal nerve ring, while the more ventral pair ari … front of the excretory pore. The
dorsal …
behind …
level of the anal ganglion. They then continue caudad, receiving … forked elements of the ventral, then of the dorsal trunk, and finally uniting near the caudal extremity. An important circumcloacal commissure arises from the anal ganglion in the male worm. Several asymmetrical commissures from the ventral to the dorsal … found along the course of these tracts. In parasitic nematodes
the labial, cervical and (in the male) …

supplied by delicate nerve termini which pierce the cuticle, the latter by a swollen end-organ lying under the cuticle. The cervical papillæ are technically referred to as *deirids*. They consist of a pair of lateral sensory organs, situated near the nerve ring.

Among the integumentary structures regarded by most nematologists as sensory or receptor organs are the *amphids*. They consist of two minute, laterally placed bodies, on the cephalic end of the worm, and externally may be pore-like, circular, spiral, helical or elongate in form. They occur commonly in free-living species and are probably also present in all or most of the parasitic species. At the caudal end of some nematodes are the *phasmids*, which helminthologists have called 'caudal papillæ' when referring to females and larval nematodes, and are also present on the male and confused with the genital papillæ. Like the amphids, they differ from tactile papillæ in having a canal and in usually being associated with a gland. The phasmids consist of a pair of lateral post-anal pores, at times elevated, connected internally with a pair of tubules, each leading to a sensory pouch irrigated by a pair of glands. They do not occur in species having caudal glands. Species with phasmids have pore-like amphids, species lacking phasmids have externally modified amphids.

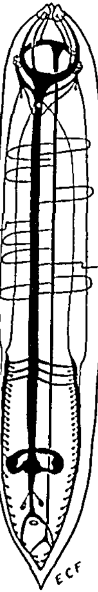


Fig. 192 Diagram of the nervous system of a male Ascaris (After Brandes.)

Typically nematodes are diecious, *i. e.*, males and females are separate individuals. In a few cases the male or the primary male sex organ is parasitic in the body of the female (syngony). Rarely parthenogenesis or syngonesis is believed to occur in parasitic nematodes, while hermaphroditism is not rare in free-living species. As a rule the male is considerably smaller than the female.

In the male the reproductive organs consist typically of a single tube differentiated into *testis* (*t*), *vas deferens* (*vd*), *vesicula seminalis* (*vs*), and *ejaculatory duct* (*ejd*). In the simplest forms this tube constitutes a straight line, in most species, however, it is coiled and convoluted back and forth many times within the body cavity. The male reproductive system opens posteriorly near the anus into the cloaca (Fig. 193). The ejaculatory duct is lined with cement or *prostate glands* (*cg*). The accessory copulatory apparatus is usually highly developed. This consists of one or a pair of *copulatory* bristles or *spicules* (*sp*), regulated by a *gubernaculum* (*gub*), while the cloaca through which both intestinal (*c*) and reproductive (*ejd*) systems discharge may be guarded by a *genital*

cone. In some groups there is a *bursa copulatrix* enveloping the posterior end of the male and serving as an organ of attachment to the body of the female during copulation. The spermatozoa are usually ameboid rather than flagellar in character, although Chitwood (1931) has found flagellate spermatozoa in the freshwater species, *Trilobus longus*. They become fully ripened only after they have been transferred to the uteri of the female.

The *vulva* or external genital opening of the female is thick-lipped and is usually ventral in position, varying in axial position from near the head to near the anus, but as a rule more commonly found in the anterior half of the body or near the equatorial plane. In a few cases there is only a single

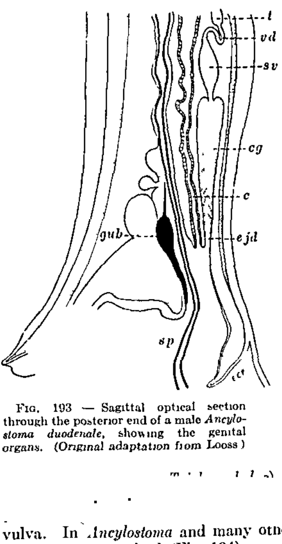


FIG. 193 — Sagittal optical section through the posterior end of a male *Ancylostoma duodenale*, showing the genital organs. (Original adaptation from Looss.)

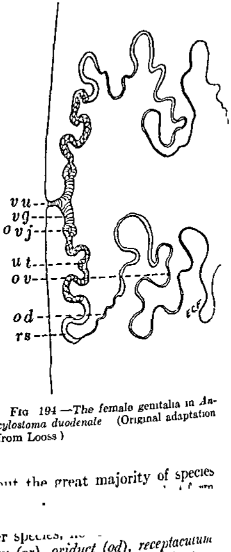


FIG. 194 —The female genitalia in *Ancylostoma duodenale*. (Original adaptation from Looss.)

... but the great majority of species

vulva. In *Ancylostoma* and many other species, ... regions are recognized (Fig. 194): *ovary* (*ov*), *oviduct* (*od*), *receptaculum seminis* (*rs*), *uterus* (*ut*), *ovejector* (*ovj*) and *vagina* (*vg*), all paired, the two ... In species such as

sn

ric

is sev...

coiling and twisting of the tubules back and forth through the body cavity. Such excessive production of the generative system may cause the intestinal tract to be displaced, or, in exceptional cases, may bring about an unusual thickening of the body.

The eggs, which are derived from a multinucleated mass of protoplasm at the inner end of the ovary and characteristically containing yolk material, pass down the lumen of the ovarian tubule, thence through the oviduct, and are fertilized *en route* through the receptaculum seminis on the way to the uterus. Here they are stored for a longer or shorter period, depending on the species. When the uterus becomes gravid, the eggs are squeezed out through the ovejector into the vulva and are laid. The egg is the most resistant stage of nematodes. It is provided with two, and at times three or more layers. The innermost layer, composed of a lipoid (probably sterol, according to Chitwood, 1938) and the shell proper or chorionic layer, consisting of chitin, are apparently secreted by the egg itself upon stimulation by the entering spermatozoon. The innermost layer, really the *vitelline membrane*, is likely the one which protects the embryo at usual temperatures but becomes permeable at higher temperatures. The shell proper is the skeletal or supportive structure. In *Ascaris* there is an outermost "albuminous" layer, which is apparently laid on as a secretion from the uterine wall. It is not essential for normal development and is lacking in the majority of nematode species. The daily output of eggs varies widely in different species, from a few dozen (as in *Strongyloides stercoralis*) to 200,000 or more (as in *Ascaris lumbricoides*). Moreover, the number of eggs produced by worms of a particular species varies with the environmental conditions in the host.

The state of development at the time of oviposition varies in different groups of nematodes but is usually related to the length of time the eggs are stored *in utero*. In *Ascaris* the egg recovered in the feces of the host is usually unsegmented. In *Trichocephalus* the first cleavage frequently takes place shortly after oviposition. The hookworm egg recovered in normally formed feces is usually 4- to 8-celled. All of these species are referred to as oviparous. Certain other species, such as the parasitic generation of *Strongyloides stercoralis*, may have embryonated eggs, with first-stage larvae almost ready to hatch when the eggs are laid. They are said to be *ovoviviparous*. In still other species, such as *Trichinella spiralis* and *Dracunculus medinensis*, the larvae have hatched previous to their escape from the mother worm. Such nematodes are spoken of as *viviparous*. In certain filarioid nematodes the egg-shell elongates *in utero* to accommodate the developing embryo, so that by the time the egg is laid it has become stretched into the shape of an enveloping sheath. Hatching, in the strict sense, does not occur until this embryonic "sheath" is shed. In *Thelazia callipaeda*, the egg-shell, after oviposition, "balloons" on one side and serves as a float for the enclosed larva.

THE LIFE CYCLES OF THE PARASITIC NEMATODES

The life cycles of parasitic nematodes include, on the one hand, types with a very simple development, and, on the other, those with a very

compl
(1931)
is about as simple as possible, considering their complexity. Yet even in the simplest life cycle one or more moults occur. Probably the simplest type in a human parasite is that of *Enterobius vermicularis*, the rhabditoid larva of which has practically completed its development within the egg at the time of oviposition, so that the accidental ingestion of this mature egg on the part of the human host provides all the conditions necessary for the hatching and development of the larva to an adult worm in the human intestine. Eggs of *Ascaris* and *Trichocephalus* require some time on the soil before the larva is sufficiently mature for hatching to take place in the human intestinal tract. In *Ascaris lumbricoides* the first moult takes place within the egg shell. Although hookworm and *Trichostrongylus* eggs occasionally hatch inside the intestine of the host, in both cases the emerging rhabditoid larva must be voided in the stool and undergo a period of growth on the soil, followed by metamorphosis into the infective-stage filariform larva, before the worm may again utilize the body of the host. *Strongyloides stercoralis*, which has not completely lost its free-living mode of life, frequently interpolates one or more complete free-living generations with its parasitic one, although it has also developed an adaptation for complete parasitic existence, whereby its rhabditoid larvæ, while still within the bowel, metamorphose into filariform larvæ, which are capable of penetrating the intestinal mucosa, and reach the lungs by an internal route of migration (*hyperinfection*). Furthermore, the spiruroid and filarioid nematodes require an arthropod intermediate host: *Gnathostoma spinigerum* necessarily utilizes a species of Cyclops as first intermediate hosts; *Wuchereria bancrofti* utilizes mosquitoes, *Loa loa* and *Onchocerca volvulus* require species of *Chrysops* and *Simulium* respectively. The first-stage larvæ of *Dracunculus medinensis* are discharged from the body of the mother worm directly into fresh water, where they are ingested by the intermediate host, Cyclops. In the case of blood-sucking fly hosts, the freely moving microfilariæ are removed from the peripheral circulation or from peripheral lesions by puncturing the skin; in the case of non-biting arthropods the larvæ are ingested by the intermediate host after active or passive escape from lesions in the definitive host. Within the intermediate host a metamorphosis of the larva takes place, usually accompanied by a process of moulting, whereupon the mature larva may, in the case of blood-sucking insects, be transferred actively to the definitive host In other cases it may become quiescent, or even become encapsulated and await passive transfer through the accidental ingestion of the larval host by the definitive host. Thus, larval development may include only a rhabditoid larva, with two or more instars; or it may also include a filariform larva as an adaptation for penetration of the skin; or it may comprehend a prelarval microfilaria, as well as successive larval types.

The routes of migration of some of the parasitic nematode species within the definitive host are likewise complicated and devious. *Gongylonema* larvæ, upon being swallowed, directly invade the epithelium of the anterior portion of the digestive tract and develop to maturity. Infective-stage larvæ of *Hæmonchus*, when swallowed by the appropriate host, become

attached to the wall of the stomach and proceed with their development Mature hookworm larvæ, as well as filariform larvæ of *Strongyloides*, usually invade the definitive host *via* the skin, and require passage through the venous circulation to the lungs, thence out into the air passages and over the epiglottis into the digestive tract, passing on into the small intestine where they complete their growth. If, however, mature hookworm larvæ are directly introduced into the intestine, they may pass through the stomach without injury and, on arrival in the posterior level of the jejunum or anterior level of the ileum, attach themselves to the mucosa and grow to adulthood. *Œsophagostomum* larvæ, when swallowed, pass through the stomach and small intestine into the colon, where they burrow into the mucosa, set up an inflammatory process, and become encapsulated, only to emerge later and become attached by their heads to the wall of the large intestine. The infective-stage eggs of *Ascaris lumbricoides* hatch normally only after passing through the stomach into the small intestine, whence the free rhabditoid larvæ penetrate through the intestinal wall into the portal circulation or the lymphatics, and, on arrival in the pulmonary capillaries, break through into the air passages, and reach the intestine again *via* the epiglottis. Larvæ of *Spirocerca lupi*, a common parasite of the dog in the Orient, frequently encountered in the Mediterranean area and occasionally in the Gulf Coast area of the Southern United States, utilize the stomach wall through which to gain entry into the blood stream In the case of *Trichinella spiralis*, the viviparous female, after copulation, bores into the intestinal glands and discharges her brood of larvæ, which pass through the mesenteric lymphatics or veins into the right heart and lungs, thence into the arterial circulation, finally coming to lodge in the muscles, where they encyst. Here they remain until the infected flesh is ingested by another host, whereupon the larvæ excyst and develop into adult worms

The position of the primitive adult nematode parasite in its definitive host was undoubtedly in the intestinal tract. Species in which the adult worms are now adapted to other organs or tissues, may have come upon their present site of residence through lodgment of the larvæ passing *en route* through such channels or by accidental migration out of customary channels. Thus, *Wuchereria bancrofti* in the lymphatics, *Dirofilaria immitis* in the right heart of the dog; *Onchocerca* in subcutaneous pockets and *Dracunculus medinensis* in subcutaneous tissues; *Spirocerca* in the wall of the aorta of the dog; *Dioctophyma renale* in the kidney or abdominal cavity; and *Trichosomoides crassicauda* in the bladder of the rat, all these species now live in foci which are evidently secondary to an original habitat in the intestine, a position that has long since been relinquished in favor of the secondary site. In *Spirocerca*, moreover, even the secondary site has been abandoned as a habitat for the development of the mature worm, a return has been made to the wall of the digestive tract, to provide for an outlet of the eggs to the outside world Finally, species in remote tissues, such as the lymphatics, having an outlet for larvæ to reach the blood, have provided most effectively for transfer of their larvæ to new hosts through the intermediary of blood-sucking insects.

Free-living species of nematodes are undoubtedly the most primitive but at the same time very considerably modified from the archetype

Steiner (1920) has made out a logical case for the common ancestry of the nematodes and the rotifers. Both groups lack a true lining to the body cavity; they have homologous digestive systems (the gizzard or mastax of rotifers being comparable to the esophageal valvular apparatus of nematodes); the male sex organs in both groups have the same fundamental arrangement; the caudal glands are comparable to the cement glands of the rotifers; the triradiate symmetry of nematodes is secondary to a more primitive bilateral one; the cervical and head papillæ of nematodes have homologues respectively in the lateral sense buds and retrocerebral organ of rotifers, and the excretory system of present-day nematodes, although lacking "flame cells" or solenocytes, is probably derived from a bilateral system, opening into a cloaca, as in the rotifers. The locomotion of nematodes appears to have been secondarily acquired. The habits and habitats of the two groups are fundamentally alike.

CHAPTER XXIII

THE NEMATODES. CLASSIFICATION

THE BASIS OF CLASSIFICATION

As the number of known species of nematodes has increased by leaps and bounds within the past several decades, the older system of classification, whereby family groups were loosely united under the general Class **Nematoda** Rudolphi, 1808, has become untenable, just as the classification of the Nematoda, Nematomorpha and Acanthocephala as major subdivisions of the Phylum Nemathelminthes is no longer justified. Moreover, increased information regarding the structure of the many species involved, and more *especially concerning the life cycles and the larval stages of these worms*, has resulted in a gradual grouping of the families into superfamilies, and these, in turn, into suborders and orders. The system which the author had adopted is in keeping with this tendency. For the most part the superfamily groupings are those of Railliet. For the more comprehensive groupings Cram's and Chitwood and Chitwood's classifications have been used. The outline of the system is as follows:

OUTLINE OF CLASSIFICATION OF THE NEMATODA

PHYLUM NEMATODA (RUDOLPHI, 1808) DIESING, 1861, EMEND. PEARSE, 1936.

Unsegmented invertebrate animals, with a fundamental bilateral symmetry, and a secondary tri-radiate symmetry of the oral end and esophagus; with three body layers; elongated, cylindrical or filiform, with a definite

Class I. Aphasmidia Chitwood and Chitwood, 1933

telogonic or hologonic; caudal glands typically present

ORDER I. CHROMADORIDA CHITWOOD, 1933

myarian. Male with 2 spicules, 1 or 2 testes; female with 1 or 2 ovaries, vagina transverse, simple. Free-living species living in moist soil or water

ORDER II. ENOPLIDA CHITWOOD, 1933

(Syns., Urolabea Carus, 1863; Axonchia Cobb, 1919; Bolbinia Cobb, 1919; Triplonchia Cobb, 1919; Alaimia Micoletzky, 1922.)

Oral opening cylindrical, subglobular, reduced or rudimentary; stylet present or absent; esophagus cylindrical, conoidal or having a narrow anterior part and a wide posterior part, both parts being extremely long and narrow (Trichinelloidea, Mermithoidea); rarely terminated by a distinct swelling. Polymyarian or rarely meromyarian. Male with 1, 2 or no spicules, 1 or 2 testes; female with 1 or 2 ovaries; vagina usually transverse, simple, at times elongated, muscular.

Suborder I. Enoplina (Filipjev, 1929) Pearse, 1936

Forms with cephalic papillæ consisting of an internal circle of papillæ or short setæ and an external circle of 6 or 10 setæ, at times in rings of 6 and 4; with amphids pocket-like or elongated; somatic setæ rudimentary, never long, narrow, cylindroidal; with or without teeth; with esophagus cylindrical or conoidal; with intestine well developed; with caudal glands usually present; sexes telogonic, with 1 or 2 gonads; male possessing 2 spicules and usually a gubernaculum; having genital papillæ or setæ at times in subventral rows, at times indistinguishable from somatic papillæ or setæ, female with short transverse vagina, usually oviparous. Free-living species living in moist soil or water.

Suborder II. Dorylaimina (Chitwood, 1933) Pearse 1936

(Syns., Trichurata Skrjabin, 1916; Trichinellida Sprehn, 1927, Trichocephalata Skrjabin and Schultz, 1928; Trichinellata Faust, 1929; Dorylaimata Chitwood; 1933.)

Forms with cephalic papillæ consisting of an inner circle of 6 or 0 and an external ci [illegible] pocket-like amphids frequently opening through a [illegible] with moutl [illegible] with esophagus having a long, narrow, anterior part and a [illegible] posterior part; with intestine either well-developed or degenerate; with caudal glands lacking, sexes telogonic or hologonic, with genital papillæ of male often arranged in 2 or more subventral rows; female having a short, [illegible] Three transverse vagina or a lon [illegible] elloidea recognized superfamilies, [illegible] Hall, 1916 and Mermithoidea Wülker, 1934. Human representatives belong to the latter two subfamilies.

Superfamily Trichinelloidea Hall, 1916

(Syn., Trichuroidea Railliet, 1916)

Anterior part of body filiform; esophagus more or less degenerate in posterior part, more or less entirely surrounded by numerous glands arranged in columnar fashion; intestine cellular; polymyarian, sexes hologonic; male spicule single or absent; female with single ovary. Two recognized families.

Family TRICHINELLIDÆ Ward, 1907

Copulatory sheath and spicule not present in male; females viviparous; adults in intestinal wall and larvæ in muscles of mammals. Human representative: *Trichinella spiralis* (Owen, 1835).

Family TRICHOCEPHALIDÆ Baird, 1853

Male with copulatory sheath and usually one spicule; female oviparous; eggs barrel-shaped, with clear polar "plugs;" adults parasitic in intestine, liver or urinary bladder of mammals and birds. Human representatives: *Trichocephalus trichiurus* (Linn., 1771); *Capillaria hepatica* (Bancroft, 1893).

Superfamily Mermithoidea Wülker, 1934

Esophagus more or less degenerate, at least posteriorly, esophageal glands numerous; intestine usually syncytial; polymyarian; sexes telogonic; male with one or two spicules. Recognized families: Mermithidæ and Tetradonematidæ. Larvæ of the former family (agamomermids) rarely and only accidentally present in human intestine as a contamination of food or water

Suborder III. Dioctophymatina (Skrjabin, 1923) Pearse, 1936

(Syns., Dioctophymida Sprehn, 1927; Dioctophymeata Petrov, 1930)

[illegible] mentary mouth and well-developed cylindrical esophagus and intestine, with labial pore-like amphids; excretory system lacking, without caudal glands; sexes hologonic, with 1 gonad; male with 1 spicule and without a gubernaculum; having tail in form of a muscular sucker; with genital papillæ indistinguishable from somatic papillæ; female with long, muscular vagina; oviparous. Only one superfamily.

Superfamily Dioctophymatoidea Railliet, 1916

Medium to large-sized nematodes; males with a bell-shaped muscular bursa, unsupported by rays, with a single copulatory spicule, eggs with thickened, pitted shells, lighter at the poles, in lumen of kidney and abdominal cavity of mammals, or intestinal tract of birds

Type Family DIOCTOPHYMATIDÆ Railliet, 1915

With the characteristics of the superfamily. Human representative: *Dioctophyma renale* (Goeze, 1782).

Class II. Phasmidia Chitwood and Chitwood, 1933

Nematodes with phasmids (*i. e.*, caudal chemo-receptors) usually well-developed; with amphids usually pore-like and labial in position, not specialized in structure; deirids usually present; excretory system usually having at least one lateral collecting duct; hypodermis possessing a dorsal, ventral and two lateral cords; gonads telogonic; caudal glands lacking

ORDER I. RHABDITIDA CHITWOOD, 1933

Oral opening usually surrounded by 3 or 6 lips; esophagus consisting of corpus, isthmus and bulb (or pseudo-bulb); excretory system with one or more lateral collecting ducts and *often* 2 subventral excretory glands; males with one or two spicules.

Suborder I. Rhabditina (Chitwood, 1933) Pearse, 1936

(Syns., Anguillulata Skrjabin, 1923; Anguillulida Oerley, 1880; Rhabdiasata Cram, 1927; *Hypophalli* (Molin, 1858) Sprehn, 1932, *pro parte*; Ascarida Sprehn, 1927, *pro parte*.)

Forms with cephalic papillæ consisting of an inner circle of 6 and an external circle of 10, 6 or 4 papillæ; amphids usually dorsolateral in position; excretory system usually H-shaped, rarely ∩-shaped; female with short, narrow vagina.

Superfamily Rhabditoidea Travassos, 1920

Stylet lacking. [illegible] habditidæ, Diplogasteridæ, S [illegible] Cephalobidæ, Angiostomatidæ, Cylindrogasteridæ, and possibly other, undesignated, family assemblages.

Species of medical importance belong to the families Rhabditidæ and Strongyloididæ.

Family RHABDITIDÆ Micoletzky, 1922

(Synonym, Rhabdiasidæ Railliet, 1915, *pro parte*)

Forms with a well-developed, three-sided, prismatic or tubular buccal cavity, usually without teeth, esophagus usually with a long cylindrical portion, a median bulbar swelling, a narrower cylindrical portion, and posterior bulb containing valves (type of esophagus referred to as "rhabditis-like" or "rhabditiform"); probably include only coprophagous species. Human representatives: *Rhabditis pellio* (Schneider, 1866); *R. niellyi* (Blanchard, 1885); *R. hominis* Kobayashi, 1914; *Turbatrix aceti* (Mueller, 1783).

Family STRONGYLOIDIDÆ Chitwood and McIntosh, 1934

Forms with an oral opening surrounded by 2 lateral lips, each bearing 2 submedian papillæ and an amphid. *Free-living generation* with a short stoma and esophagus with valvulated bulb; males with a single testis, 2 arcuate, equal spicules and gubernaculum, and without caudal alæ; females with 2 divergent uteri and reflexed ovaries. *Parasitic females* with greatly reduced stoma and long narrow esophagus; *parasitic males* either similar to free-living males or, if tissue parasites, filiform, rarely found. Human representative: *Strongyloides stercoralis* (Bavay, 1877).

Superfamily Tylenchoidea, Chitwood and Chitwood, 1937

(Syn., Anguillulinoidea Pereira, 1931-1932)

Forms differing from the Rhabditoidea primarily in the presence of an

oral stylet; parasitic in vegetable tissues. All species which have been reported from man (*i. e.*, "spurious" parasites) belong to the

Type Family TYLENCHIDÆ Micoletzky, 1922

(Syn. Anguillulinidæ Baylis and Daubney, 1926)

Small, free-living, semiparasitic or parasitic species, having a pharynx in the adult modified into a protrusile spear; esophagus simple or with a median and a posterior bulb-like swelling. The adults, larvæ or eggs of those forms parasitic in vegetable tissues or saprozoic in decaying vegetation have at times been reported as parasites of the human intestinal tract, but such a condition is purely accidental. The following identified species have been reported from man: *Tylenchus putrefaciens* Kuehn, 1879; *Heterodera marioni* (Cornu, 1879) Goodey, 1932.

Suborder II. Strongylina (Railliet and Henry, 1913) Pearse, 1936

(Syns., Sclerostomata Rudolphi, 1809; Bursata Vera Leiper, 1911; Strongylida Sprehn, 1927, Strongylata Railliet and Henry, 1913)

Forms having oral opening surrounded by 3, 6 or no lips, usually indistinct; with an inner circlet of 4 to 10 papillæ; with excretory system composed of lateral collecting ducts and subventral excretory cells. Bursate nematodes, the membraneous bursa supported by a system of six-paired and one or two dorsal rays; males with two spicules and females usually with two ovaries, and either a muscular vagina and/or a highly developed ovejector. Musculature polymyarian or meromyarian.

Superfamily Strongyloidea (Weinland, 1858) Hall, 1916

Mouth opening usually large, often surrounded by a corona radiata; cephalic papillæ at times setose, meromyarian; male with broad, conspicuous bursa traversed with typical rays; copulatory spicules typically two; ovary single or double; buccal capsule usually well-developed in both sexes; rhabditoid larvæ develop in moist earth. Human representatives belong to the following three families.

Family STRONGYLIDÆ Baird, 1853

Buccal capsule wide, without teeth or cutting plates but with a ring of chitinous armature, bursa and two equal spicules present; usually parasitic in alimentary canal of vertebrates. Human representatives: *Ternidens deminutus* (Railliet and Henry, 1905); *Œsophagostomum apiostomum* (Willach, 1891), *Œ. stephanostomum* var. *thomasi* Railliet and Henry, 1909

Family SYNGAMIDÆ Leiper, 1912

Buccal capsule well-developed, without conspicuous teeth, but with a thickened chitinous rim, bursa short, spicules usually equal, stout; parasites of the respiratory system. Human representative: *Syngamus laryngeus* Railliet, 1899.

Family ANCYLOSTOMATIDÆ (Looss, 1905) Lane, 1917, emend. Nicoll, 1927

Buccal capsule well-developed and armed, bursa large, with well-

developed rays; uteri divergent; parasites of the alimentary canal of vertebrates. Human representatives: *Ancylostoma duodenale* (Dubini, 1843); *A. caninum* (Ercolani, 1859); *A. malayanum* (Alessandrini, 1905); *A. braziliense* Gomez de Faria, 1910; *Necator americanus* (Stiles, 1902).

Superfamily Trichostrongyloidea Cram, 1927

Mouth reduced; corona radiata lacking; buccal capsule absent or rudimentary; cephalic papillæ never setose; meromyarian or polymyarian; relatively slender forms, but with bursa not reduced in size. All species of this superfamily recorded from man belong to the

Type Family TRICHOSTRONGYLIDÆ Leiper, 1912.

Bursa large, with well-developed rays; buccal capsule absent; cutting organ, if present, consisting of a single lancet; uteri divergent; parasitic in alimentary canal of ruminants. Human representatives: *Trichostrongylus columbriformis* (Giles, 1892); *T. probolurus* (Rail., 1896); *T. vitrinus* Looss, 1905; *T. orientalis* Jimbo, 1914, and several other species of this genus; *Hæmonchus contortus* (Rud., 1803); *Mecistocirrus digitatus* (v. Linst., 1906).

Superfamily Metastrongyloidea (Lane, 1917) Cram, 1927

Mouth reduced, simple, directed straight forwards; corona radiata lacking; cephalic papillæ never setose; capsule lacking or only slightly reduced; polymyarian; bursa with true but rather stunted, atypical rays; uteri convergent; parasitic in respiratory or circulatory system, or in cranial sinuses of mammals. The species reported from man belongs to the

Type Family METASTRONGYLIDÆ Leiper, 1907

With the characters of the superfamily. Human representative: *Metastrongylus elongatus* (Dujardin, 1845).

Suborder III. Oxyurina (Cram, 1927) Pearse, 1936

(Synonyms, Oxyurata Cram, 1927, Ascarida Sprehn, 1927, *pro parte*; Hypophalli (Molin, 1858) Sprehn, 1932, *pro parte*; Ascaridata Skrjabin, 1915, *pro parte*.)

Forms with cephalic papillæ consisting of an inner circlet of 6 papillæ and an outer circlet of 8; amphids pore-like; excretory system ⋂-shaped or H-shaped with short anterior tubules; meromyarian; males with one spicule (exceptionally two or none), imperfectly chitinized; females oviparous; eggs flattened on one side; forms monoxenous.

Type Superfamily Oxyuroidea Railliet, 1916

Small nematodes, pin-shaped, with buccal capsule; and with cuticular lining of esophagus well-developed; deirids lacking; males without a true bursa or with a poorly-developed one, but with a posterior papilla or caudal projection; copulatory spicules one or two; ovaries one or two; females

... dæ,

... belong to the

Atractidæ and Rhigonematidæ. Species of medical interest

Type Family OXYURIDÆ Cobbold, 1864.

With the characteristics of the superfamily; male with a single spicule or two equal spicules. Human representatives: *Enterobius vermicularis* (Linn., 1758): *Syphacia obvelata* (Rud., 1802).

Suborder IV. Ascaridina (Railliet and Henry, 1915) Pearse, 1936

(Synonyms, Ascarida Sprehn, 1927, *pro parte;* Hypophalli (Molin 1858) Sprehn, 1932, *pro parte;* Ascaridata Skrjabin, 1915, *pro parte;* Ascaridata [illegible]

[illegible]

single papillæ; mouth typically with three lips; buccal capsule lacking; meromyarian or polymyarian; males with two spicules; females usually with two ovaries, occasionally more than two; oviparous; forms usually monoxenous, but at times complicated by a larval migration through the body of the host.

TYPE SUPERFAMILY ASCARIDOIDEA RAILLIET AND HENRY, 1915

Usually fairly large or stout nematodes; mouth commonly provided with three conspicuous lips but without buccal capsule; lining of esophageal corpus usually lacking cuticular thickening; deirids usually present; males usually without caudal alæ, with only one or two copulatory spicules; females with two ovaries, oviparous; development direct, usually without an intermediate host.

This type superfamily includes the families Ascarididæ, Heterakidæ, Cosmocercidæ and Kathlaniidæ. Species of medical interest belong to the

Type Family ASCARIDIDÆ Baird, 1853.

Male with two spicules; uterine branches parallel; eggs very numerous, unsegmented when laid. Human representatives: *Ascaris lumbricoides* Linn., 1758; *Toxocara canis* (Werner, 1782); *T. cati* (Schrank, 1788); *Lagochilascaris minor* Leiper, 1909.

ORDER II. SPIRURIDA CHITWOOD, 1933

Oral opening surrounded by 2 lateral pseudolabia or 6 rudimentary labia, or without labia; at times 2 lateral "jaws;" esophagus consisting of an anterior muscular and a posterior glandular part; excretory system with 2 posterior ducts and lacking subventral excretory cells; males with 2 spicules, caudal alæ, if present, never bursate; vagina of female well-developed; females oviparous or viviparous. Two suborders are recognized, the Spirurina and the Camallanina. Species of medical interest are found in both suborders.

Suborder Spirurina (Railliet and Henry, 1915) Pearse, 1936

Synonyms, Filariata Skrjabin, 1915; Filarida Sprehn, 1927; Spirurata Railliet and Henry, 1915)

Body usually long and slender; mouth fundamentally with two pseudolips or without lips, and surrounded by papillæ or other oral structures.

esophagus slender; polymyarian; female larger than male; vulva present or absent; two, *four or more uteri*, *rarely one*; heteroxenous larvæ in intermediate hosts.

Superfamily I. Spiruroidea Railliet and Henry, 1915

Filiform or fairly stout worms; mouth without lips or with two or more pseudo-lips which bound the buccal cavity; intestine simple, without diverticula; caudal alæ usually present in male; spicules two, frequently unequal; *vulva usually near the middle of the body*; parasites of the alimentary tract, respiratory system, or orbital, nasal or oral cavities of vertebrates. Human representatives are found in the families Spiruridæ, Gnathostomatidæ, Physalopteridæ, Thelaziidæ and possibly the Acuariidæ.

Type Family SPIRURIDÆ Oerley, 1885

Mouth usually with two or four trilobed, lateral pseudo-lips, occasionally accessory dorsal and ventral lips; chitinized vestibule in front of esophagus; caudal alæ of male well-developed, supported by pedunculated papillæ; vulva of female near the middle of the body; oviparous, parasitic in the tissues of the mouth, esophagus, stomach, and intestine of vertebrates. Human representative: *Gongylonema pulchrum* Molin, 1857 (syn. *G. subtile* Alessandrini, 1914; also *G. hominis* Stiles, 1921).

Family GNATHOSTOMATIDÆ Blanchard, 1895

Mouth with two large, trilobed, pseudo-lips; whole or anterior part of body covered with minute, ramified spines; male with caudal alæ supported by broad pedunculated papillæ; copulatory spicules equal or unequal; female with vulva posterior to middle of body; uterine tubes two *or four*, oviparous; eggs with thin shells, with external pitting; parasitic in wall of intestine of fishes, reptiles and mammals. Human representatives. *Gnathostoma spinigerum* Owen 1836; *G. hispidum* Fedtsch., 1872.

Family PHYSALOPTERIDÆ Leiper, 1908

Mouth with two large, simple, triangular, pseudo-lips, armed internally with one or more teeth; cuticle reflected forwards over the lips to form a cephalic collarette; bursal alæ with supporting papillæ in form of lanceolate expansion; caudal papillæ pedunculated; parasitic in alimentary canal of vertebrates. Human representative: *Physaloptera caucasica* v. Linstow, 1902.

Family THELAZIIDÆ Railliet, 1916

Mouth without definite lips, or with inconspicuous pseudo-lips; short buccal capsule usually present; caudal extremity of male with or without alæ, [illegible] pillæ; vulva of female anterior or poste[illegible] orbital, nasal or oral cavities of mammals or birds, in the air sacs o[illegible], or the intestine of fishes. Human representatives: *Thelazia callipæda* Railliet and Henry, 1910, *T. californiensis* Kofoid and Williams, 1935.

Superfamily Filarioidea (Weinland, 1858) Stiles, 1907

Filiform worms; mouth usually simple, circular or somewhat dorsoventrally elongated, surmounted by an internal circlet of 4, 2 or 0 papillæ and an external circlet of 8 papillæ; without lips; buccal cavity lacking or rudimentary; esophagus cylindrical, frequently divided into two parts; intestine simple, sometimes atrophied posteriorly; males with or without caudal alæ; copulatory spicules usually unequal and dissimilar; vulva of female almost always in esophageal region; parasitic in the circulatory, lymphatic, muscular, or connective tissues, or in the serous cavities of vertebrates.

This superfamily contains the following families: Filariidæ, Acanthocheilonematidæ, Desmocercidæ and Stephanofilariidæ. Species of medical interest are included in the family Acanthocheilonematidæ.

Family ACANTHOCHEILONEMATIDÆ Faust, 1939

(Synonyms, Dirofilariidæ Sandground, 1921; Dipetalonematidæ Wehr, 1935)

Mouth circular or dorsoventrally elongated; cephalic papillæ consisting of an external circlet of 8 papillæ and an internal circlet, if any, of internolaterals only; esophagus at times divided into two morphologically distinct parts; caudal alæ of male usually lacking or very narrow; spicules usually unequal and dissimilar; females give birth to slender microfilarial embryos, which are aspinose.

Subfamily Acanthocheilonematinæ Faust, 1939

(Synonyms, Onchocercinæ Leiper, 1911, *pro parte;* Loainæ Yorke and Maplestone, 1926, *pro parte;* Setariinæ Yorke and Maplestone, 1926, *pro parte;* Dipetalonematinæ Wehr, 1935).

Forms with caudal alæ either lacking or extremely narrow. Human representatives: *Wuchereria bancrofti* (Cobbold, 1877); *Onchocerca volvulus* (Leuckart, 1893); *Acanthocheilonema perstans* (Manson, 1891); *A. streptocerca* (Macfie and Corson, 1922); *Mansonella ozzardi* (Manson, 1897).

Subfamily Dirofilariinæ Wehr, 1935

(Synonym, Loainæ Yorke and Maplestone, 1926, *pro parte*)

Forms with caudal alæ well-developed, supported by preanal and postanal, pedunculated papillæ. Human representatives: *Dirofilaria magalhæsi* (Blanchard, 1896); *D. repens* Railliet and Henry, 1911; *Loa loa* (Cobbold, 1864).

Suborder II. Camallanina (Chitwood, 1936) Pearse, 1936

Oral opening usually without pseudo-labia; mouth at times formed by 2 lateral "jaws;" esophageal glands usually uninucleate. The following two superfamilies are recognized.

Superfamily Camallanoidea Travassos, 1920

Forms having internal circlet of cephalic papillæ reduced; mouth usually well-developed. No human representative

Superfamily Dracunculoidea Cameron, 1934

Mouth a simple pore, surrounded by an inner circle of 4 to 6 papillæ and an outer circle of 4 double papillæ, and with the amphids posterior to the lateral papillæ; esophagus and intestine rudimentary; vulva in middle of body, atrophying before sexual maturity; uteri divergent. Larvæ "rhabditoid." With two recognized families, Dracunculidæ and Philometridæ. Human representative is found in the

Type Family DRACUNCULIDÆ Leiper, 1912.

(Synonym: Fuelleborniidæ Faust, 1929)

Females enormously longer than males; anus and vulva atrophied in gravid females, which discharge their larvæ through a rupture of the body-wall near the mouth; viviparous; parasitic in connective tissue and body cavities of vertebrates. Human representative: *Dracunculus medinensis* (Linn., 1758) Gallandant, 1773.

CHAPTER XXIV

THE APHASMID NEMATODE PARASITES OF MAN

SUBORDER DORYLAIMINA (CHITWOOD, 1933) PEARSE, 1936

(Synonyms, Trichurata Skrjabin, 1916; Trichinellata Faust, 1929)

(TRICHINELLA, TRICHOCEPHALUS AND RELATED FORMS)

THE aphasmid nematodes, as designated by Chitwood and Chitwood, 1933, include among others those species which are here grouped in the superfamily **Trichinelloidea Hall**, 1916 and the superfamily **Mermithoidea Wülker**, 1934. All of these forms are characterized by having a filiform body, at least in its anterior portion, and by having an esophagus with a long, narrow, anterior part and a narrow or wider posterior part. They have pocket-like amphids and lack caudal glands. The superfamily **Trichinelloidea** contains three genera parasitic in man, *Trichinella*, *Trichocephalus* and *Capillaria*, each of which is represented by a single species in man. The mermithoid nematodes are occasionally accidental contaminators of the human body during their larval stage.

SUPERFAMILY TRICHINELLOIDEA HALL, 1916.

The species of this group have a complete intestinal tract with an anal opening. The females have a relatively straight, bluntly rounded posterior end, while the males are curved ventrad and possess either a single spicule or none at all. The females have but a single ovary. The family **Trichinellidæ** contains one and the family **Trichocephalidæ** contains two of the three species parasitic in man.

Family TRICHINELLIDÆ Ward, 1907

This family was created for a single species, *Trichinella spiralis*, in which the posterior end of both the males and females is only slightly thicker than the anterior end. The male lacks a copulatory spicule and sheath. The female is viviparous.

GENUS TRICHINELLA RAILLIET, 1895

(genus from θρίξ, thread)

Trichinella spiralis (Owen, 1835) Railliet, 1895. (The trichina worm.)

Synonyms. *Trichina spiralis* Owen, 1835, *Trichina affinis* Diesing, 1851, *pro parte*, *Trichina spiralis hominis* Kraemer, 1853, *Pseudalius trichina* Davaine, 1862

Historical and Geographical Data.—*Trichinella spiralis* was first observed in the larval stage, encysted in the muscular system of patients who came to autopsy in London (Peacock, 1828, Hilton, 1833). The larvae were again found in London (Paget, 1835) at the autopsy of an Italian who had died of tuberculosis. They were referred to Owen, who described the worms and named them *Trichina spiralis*. Soon afterward other cases of human infection were reported from England, Ger-

many, Denmark and North America. In 1846, Leidy (Philadelphia) first recorded the presence of the larvæ in the flesh of pigs. The researches of Leuckart (1855) and Virchow (1859) showed that *Trichinella* larvæ, when fed to an appropriate experimental animal, became adult in a few days, and that the females were viviparous. Zenker (1860) first demonstrated that *Trichinella* infection in man was a serious disease. This led to renewed efforts on the part of German investigat...

...cooked. Brown (1897) found that hypereosinophilia was clinically very suggestive of trichinosis. The disease, which was proved to be both endemic and epidemic in its nature, and to be potentially capable of producing a high mortality, became an important public health problem and led not only to careful epidemiological surveys but to inspection of meats and to other precautions to reduce the source of human infection.

In 1898 Osler reported a 0.6 per cent infection in routine examination of diaphragms at autopsy in the Johns Hopkins Hospital (Baltimore). Ransom (1915) found 1575 cases reported from the United States between 1842 and 1914, with 240 deaths (15 4 per cent). More recently Sawitz (1938) surveyed the literature from 1915 through 1936, which revealed 2968 cases, with reported deaths slighty under 5 per cent. In the United States there has thus been an increased number of recognized cases in recent years but a considerably lower mortality rate. The states with the highest morbidity rates (1930–1936) are California, Maine, New York, Connecticut, and Massachusetts, while N
South Dakota and Oregon have
rarely reported from the Southern
found 6 per cent infection in the
cent in an Alabama autopsy series of 100 cases, none of whom gave a clinical history of trichinosis.

The incidence of trichinosis in the United States in recent years, as determined from 5313 post-mortem examinations, averages 16.1 per cent (Wright, Jacobs and Walton, 1944). Special necropsy surveys conducted since 1930 have provided the following percentage range of infection: Boston, 18.6 (digestion technic, Queen, 1931), Minneapolis, 17.1 (pressed muscle, Riley and Scheifley, 1934); San Francisco, 24.0 (digestion, McNaught and Anderson, 1936); Washington, D.C., 13.6 (digestion and compression, Hall and Collins, 1937); Alabama, 33.0 (digestion and compression, Walker and Breckenridge, 1938); New Orleans, 6.0 (digestion, Sawitz, 1939); Durham, N. C., 2.8 (digestion and compression, Harrell and Johnston, 1939); Dayton, O., 20.1 (digestion, Oosting, 1940); Detroit, Mich., 18.6 (digestion and compression, Gould, 1940); Nashville, Tenn., 10 0 (digestion and compression, Meleney, 1941); Richmond, Va , 6.0 (digestion and compression, Broders and Porter, 1944), and Northern Utah, 0 (Merrill, 1941).

Trichinosis is extensively distributed but in recent decades the incidence is relatively light in Germany, Spain, Hungary, and the lower Danube countries. An epidemic outbreak of trichinosis occurred in certain districts of Sweden in 1944 (Roth, 1 ... necropsies in
Holland numbering 1001 rev
than one million slaughtered
Meer, de Graaf and Brug, 1941). It occurs in Syria and India, but elsewhere in Asia human infection is negligible. Although reported from Kenya, Uganda, Tanganyika and British Nigeria, it is apparently a rela-

tively rare infection in other parts of Africa. In Mexico, D. F., Mazzotti and Chavira (1943) showed that human infection amounted to 8.5 per cent or more. In Latin America autochthonous cases have been reported from Brazil, Venezuela (Vogelsang, 1946), Guatemala (Penagos, 1944) and Chile (12.5 per cent in Santiago). It is unknown in native populations of the Philippines, Puerto Rico, Panamá and is probably not endemic in Australia (Bearup, 1937). In Hawaii Alicata (1942) has reported a 7.4 per cent incidence on the basis of random sampling of diaphragms at necropsy.

Stoll (1947) has estimated the world incidence of trichinosis to be 27.8 millions, of whom three-fourths have been assigned to North America.

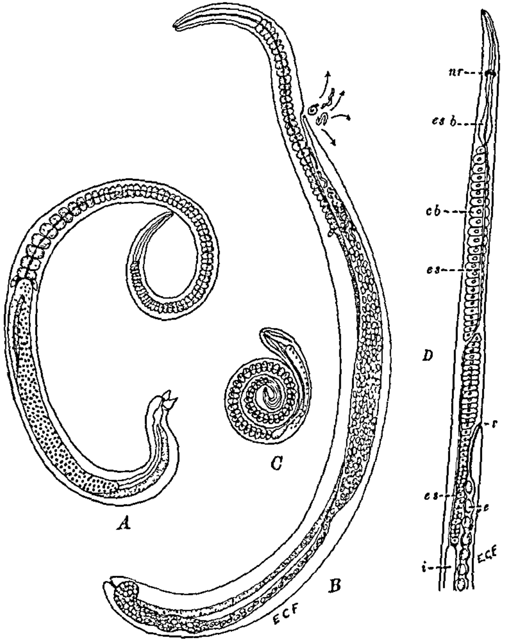
Structure of the Adult Worm and the Life Cycle.—The male worm (Fig. 195 *A*) has a length measurement of 1.4 to 1.6 mm. and a greatest transverse diameter of 40 to 50 μ. It is more attenuate anteriorly and more fleshy posteriorly. The cloaca opens at the posterior end of the worm; it is evertible during coitus; it is guarded by two conspicuous conical papillæ. The female (Fig. 195 *B*) measures 3 to 4 mm. in length and has a greatest transverse diameter about one and a half times that of the male. The adult worms are attached to or buried in the mucosa, typically of the duodenum and jejunum. Here the males impregnate the females shortly after maturing and thereafter soon die. The females then increase to their maximum size, and bore more deeply into the mucous membrane or into the villi, or may occasionally even work their way through the intestinal wall to the peritoneum or mesenteric lymph glands. By this means the viviparous young are deposited in the lymphatics, and probably also in the mesenteric veins.

Chitwood (1930) made a careful study of the esophagus of *T. spiralis* adults and was able to demonstrate the following points (illustrated in figure 195 *D*). From the oral opening to the nerve ring (*nr*) the esophagus is capillary. Thereafter it enlarges somewhat into a pseudo-bulb (*es b*). Immediately posterior to this enlargement it again becomes constricted and proceeds backwards as a capillary tubule along the side of the many body cells which are stacked on top of one another. Some little distance behind the vulva in the female and at a similar level in the male the esophagus terminates and the midgut begins. Although the esophagus is essentially non-muscular, this is more apparent than actual, since there are delicate muscle elements along its length.

According to Leuckart, as many as 1500 larvæ are deposited by each female. These larvæ at first measure 90 to 100 μ in length by 6 μ in diameter and are capable of passing both the hepatic and pulmonary filters during the period of migration. Between the seventh and the twenty-fifth day after infection they are found in the arterial circulation, through which they migrate to all parts of the body, including the myocardium, but they are capable of developing further only in striated muscle. The first larvæ reach their destination about the ninth day after infection. There follows a continuous stream of migrating larvæ for as long as the female worms are alive in the intestine, varying from a minimum of four weeks to as long as fifty-four days in the human subject (Stryker, 1947). During the period of migration the larvæ can be detected in centrifugalized samples of peripheral blood.

On arriving in striated muscle from the adjacent capillaries, the larvæ

become coiled up (Fig. 195 *C*), grow to a length of 0.8 to 1.0 mm., and provoke tissue reaction which results in their encapsulation. Fernández Ballas (1945) states that the inflammatory process involves primarily the sarcolemma of the muscle fibers immediately adjacent to the larvæ, with



as the distended uterus to the vulvar opening in the anterior fifth of the body. [illegible] anterior end of female worm, showing in partı[illegible] esophagus; *cb*, cell body; *e*, embryo *in utero*; *es*, [illegible] *i*, midgut; *nr*, nerve ring, *v*, vulva. *A* and *B*, × 90 [illegible] Parasites of Vertebrates); *C*, × 660. (Adapted from [illegible] from Chitwood.)

hypertrophy and hyperplasia, fragmentation of the fibers and the laying down of the primary (inner) capsular membrane. Then a secondary (outer) adventitious membrane is formed from the endomysium; this is infiltrated with blood capillaries. Wantland, Bardes and Levine (1945) agree that the enveloping wall is a host-tissue response to irritating metabolites of the larvæ and is not secreted even in part by the parasite. The long axis of the capsule parallels that of the muscle fibers. The capsule is an adventitious ellipsoidal object with blunt ends (Fig. 196); it is considerably larger than the larva which is tightly coiled up inside. While encapsulation may take place in any striated muscles in the body, the larvæ appear to have a particular predilection for the diaphragm, the muscles of the larynx,

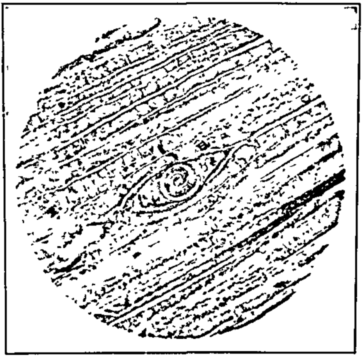


FIG. 196 Encysted trichinella larva in striped pork muscle (From Aldridge, Am. Jour Med Sci., in Craig and Faust's *Clinical Parasitology*)

tongue, abdomen and intercostal spaces, as well as the biceps, psoas, pectoral and deltoid muscles (*e. g.*, those muscles which are characterized by constant activity and are poor in glycogen), in which they are numerous near the points of tendinous attachment. According to Lewis (1928) insulin increases and dextrose decreases the number of larvæ which become encapsulated. Following encapsulation the larvæ may remain viable for many years. Such larvæ have been found in the pig eleven years and in man twenty-five to thirty-one years after exposure to infection. Larvæ which have reached their position in the striated muscles but have not yet become encapsulated are also capable of developing to maturity upon reaching the gut of suitable mammals. Frequently the larvæ undergo a

process of calcification from six to nine months after encapsulation. Usually the capsules alone become impregnated with lime, beginning at the poles where calcification is heaviest and extending towards the middle, finally providing complete sarcophagi for the young worms, and thus effectively protecting the host tissue from their toxic by-products. Calcification may also involve the larvæ themselves or the larvæ may become calcified

	Biology of Trichinella		*Pathology and Symptomatology*
INCUBATION	Larvæ become excysted in stomach →	Hours 4	
		8	
		12	
		16	
		20	
	Young worms become sexually	Days 1	← Gastro-intestinal symptoms
	differentiated →	2	Delayed-type intradermal test positive
	Young females fertilized →	3	
	Females invade intestinal mucosa	4	
	and begin to larviposit →	5	
	Larvæ begin to pass into lymphatics and blood stream en-route to skeletal muscles →	6	
		7	← Edema of face
		8	
		9	
ACUTE STAGE	Maximum invasion of muscle fibers →	10	← Fever at maximum (40 41° C.)
		11	← Myositis and "rheumatic" pains
		12	
		13	
	Decrease in larvipositing →	14	← Eosinophilia initiated
		15	← Slide precipitin test positive
	Larvæ in muscles mature but not	16	
	yet encapsulated →	17	
		18	
		19	
		20	← Eosinophilia *reaches maximum*
	Encapsulation under way →	21	← Immediate-type intradermal test positive
		22	
		23	
	Blood stream practically free of	24	
	larvæ →	25	
		26	← Respiratory symptoms
		27	
		28	
		29	
CHRONIC STAGE	Encapsulation practically complete →	Months 1	← Precipitin test positive
		2	← Fever subsides
	Maximum life of mother worms in intestinal wall →	3	← Neurotoxic symptoms and possible myocarditis
		4	
		5	
	Calcification of cysts begins →	6	← Slow convalescence
		7	
		8	
		9	
		10	
		11	
	Calcification of cysts practically complete →	Years 1	
		2	
		3	
		4	
		5	
	Larvæ possibly still viable within calcified capsules →	6	

FIG. 197.—Synoptic diagram, illustrating the progressive development of *Trichinella spiralis* and the parallel clinical picture in the patient. (Adapted from Cameron.)

without involvement of the cyst. Calcification is accelerated by feeding irradiated ergosterol and calcium lactate, but a therapeutic amount of calcium is not tolerated by the host (Wantland, 1934, 1938).

Viable *Trichinella* larvæ in infected flesh, upon being ingested by the human or other appropriate host, are digested out of their capsules in the medium of gastric juice and pass through to the duodenum, where they become encysted. Some of them become attached to the wall and, after apparently four ecdyses (Kreis, 1937), soon grow to adulthood. If adult females are not favorably situated for the deposition of their larvæ into lymph or venous channels, the larvæ may escape into the intestinal lumen and be passed in the feces.

The interrelation of the developmental stages of the parasite in the host's body and the corresponding stages in the pathology and symptomatology produced is represented in Fig. 197.

Epidemiology.—Two hosts are required for the complete life cycle of *Trichinella spiralis*, each host harboring both the definitive and the larval stages of the worm. In Nature the black rat and the brown rat are the common reservoir hosts of the parasite, which is propagated by their cannibalistic habits. Pigs, wild boars, dogs (in Manchuria, Yugawa, 1934; in New Orleans, Sawitz, 1938), cats, foxes (Lehmensick, 1942), bears (Westphal, 1943), martens, and the mongoose (Alicata, 1938), which feeds on rats, may contract the infection from the rodent reservoirs. Finally, man becomes infected most frequently from consuming infected hog flesh, although at times one to several cases are reported which have contracted the infection from eating bear meat. In Syria epidemics of trichinosis have resulted from consuming the flesh of wild boars. Chickens are rarely infected, while cuckoos and doves fail to maintain the muscle infection beyond the first few weeks after experimental feeding (Matoff, 1939). The infection has been reported from reservoir hosts from practically all countries throughout the world. The following percentage figures reflect the amount of infection in reservoirs in some countries: *hogs*, United States, 1.5; Canada, 0.57; Copenhagen, 0.00075; Germany, 0.05-0.1; Poland, 0.05; Bulgaria, 0.02-0.11; Roumania, 0.15; Lebanon, 0.54-1.3; Chile, 0.1 in the north, 6.0 in the south; Ecuador, 0.01; Hawaii, wild hogs, 15.0, *rats*, Chile 5.0-7.88

Under the artificial conditions developed by man for raising and fattening hogs, garbage containing unsterilized hog scraps is frequently fed. This probably constitutes the most common source of trichinous pork in the United States at the present time. Unprocessed or inadequately processed pork, especially in the form of "country sausage," constitutes the source of human infection. In the large slaughter houses infected meat is pooled with a hundred or more fold of uninfected meat, thus diluting the infection correspondingly and making for low-grade, usually subclinical, infections. On the other hand, infected, country-slaughtered hog flesh is usually undiluted and is responsible for a relatively small number of severe clinical infections

Several epidemics of trichinosis have occurred in the United States since 1930. One involved a college group in Iowa; another developed in a university group in Arizona, one developed in a youths' camp in New

England, and two of great severity afflicting large groups of persons were recorded for prisoner-of-war camps, one in New Mexico and one in Michigan, during the years 1942–1943. Many other epidemics of greater or lesser clinical importance are reported from time to time for small groups from all parts of the country except the Southeastern States.

Sawitz (1938) estimated that sixteen million persons in the United States are infected with *Trichinella spiralis*. However, a large proportion of these individual have no clinical history of trichinosis. Exposure to infection in the United States is not correlated with race, sex, civilian or

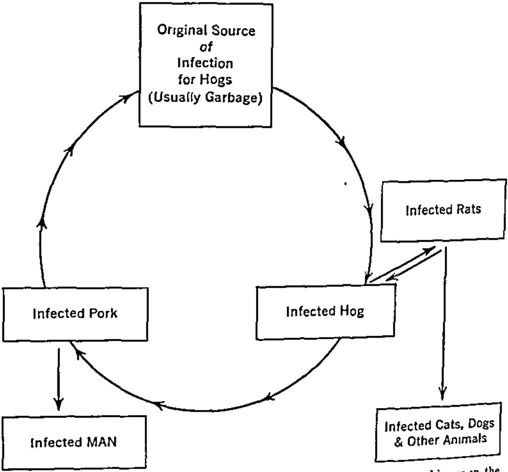


FIG. 198 —Diagram illustrating the common methods of exposure to trichinosis in the Continental United States.

military status, occupation, mental hospitalization, urban or rural residence or social-economic condition. It rises steadily from 1.2 per cent in children of one to four years of age to 19.1 per cent in the 65- to 74-year groups, then declines slightly in aged persons (Wright, Jacobs and Walton 1944).

Between January and mid-May, 1947 an epidemic of peculiar type occurred in Greenland, with 300 cases and 33 deaths, ranging in age from 2 to 63 years. In some patients the onset was sudden, in others it was gradual. Characteristically there were lassitude, diarrhea, sore throat, headache, myositis of the limbs and trunk, edema of face and limbs, and

slight fever. Severely ill individuals had an acute onset of chills and fever, vomiting and profuse diarrhea. About 80 per cent had an urticarial rash. Examination of the blood showed a high eosinophilia. There was no evidence that the disease was contagious, but eating of walrus meat was found to be responsible. A diagnosis of trichinosis was made on the symptoms commonly demonstrated by the patients, the high eosinophilia, the positive intradermal and serological tests using trichina antigen, and the demonstration of Trichinella larvæ in muscle samples of one patient who suc

The a

sources

Patho

trichiniasis, or, more familiarly, trichinosis, may be divided into three stages: (1) the period of invasion of the host (*incubation*), (2) the period of migration of the larvæ (*acute stage*), and (3) the period of encystment and tissue repair (*chronic stage*).

During the *first period* the symptoms are primarily gastro-intestinal, consisting of nausea, vomiting, diarrhea or dysentery, colic, and profuse sweating. They are due to intense catarrhal inflammation of the intestinal tract and, at times, profuse hemorrhage produced by the invading immature and the adult worms. This occurs through the seventh day, when

iatic muscular pains,

r.

myositis, involving the

intense. At times maculate or maculopapulate exanthemata, bright scarlet in color, may develop on the trunk or extremities. Typically hypereosinophilia rapidly develops and leukocytosis may be pronounced. There is frequently an elevation of temperature to 40°C. and occasionally even to 41°C. The fever is usually remittent. These symptoms occur roughly about the second week.

The *third period* is the critical one. There is characteristically an edema, particularly of the face, and especially around the eyes, sides of the nose, temples and the hands, or dehydration may be extreme. Even in the absence of other characteristic symptoms the eyes manifest a yellowish bulbar chemosis, with edema of the conjunctivæ (Lehrfeld and Breisacher, 1940). Marked cachexia may develop, due to absorption of toxins from the larvæ In grave cases delirium, cardiac and pulmonary decompensation supervene, or the patient may succumb to a complication of lobar pneumonia, pleurisy, peritonitis or nephritis.

According to McNaught (1938) "there is an active focal cellular infiltration of the myocardium, with lymphocytes, eosinophils and polymorphonuclears, with necrosis and fragmentation of the muscle fibers apparently caused by the migrating larvæ," which have never been found to encyst in this tissue. Thus, "myocarditis is one of the most serious, and not so uncommon complications of trichinosis." Blumer (1936) states that myocardial damage may produce edema, congestive hypertension, hemorrhage

of the eyes, lungs and digestive tract, while the circulating larvæ may cause thrombosis and embolism or hemoptysis.

Nervous disorders during the chronic period include peripheral neuritis, ocular disturbances, deafness, delayed or lost reflexes, restlessness, disorientation, hemiplegia, diplegia, hallucinations, delirium, meningitis and encephalitis. Amyotrophic lateral sclerosis has also been reported. Rarely thrombophlebitis and thromboenteritis have been observed. In about one-half of the cases there is a lemon-yellow chemosis of the conjunctiva.

While the symptoms *mentioned above are frequently characteristic of* clinical trichinosis, the onset and progress of the disease may at times be sufficiently atypical to lead to an inaccurate diagnosis. For example, the absence of eosinophils in the circulating blood may suggest that the symptoms are not of parasitic origin. Furthermore, in the great majority of persons exposed to light infection, there may be no clinical evidence of the disease.

Histologically, the muscle fibers immediately surrounding the invading and encysting larvæ degenerate, the transformation consisting in the loss of the transverse striæ and an increase in *the number of nuclei.* The growth of the larvæ results in the swelling of the adjacent muscle fibers, thickening and modification in structure of the sarcolemma, and prolifera*tion of the intermuscular tissue.* The *larvæ attain a length of* 0.8 to 1 mm., their growth being at the expense of the surrounding muscle fibers which gradually become absorbed, while the hyperplastic connective tissue *produces the capsule. Calcification is the final outcome* of the invasion of fat cells at the poles of the capsules.

Diagnosis.—On inquiry of the average case of clinical trichinosis the *patient will give a history of having eaten pork* inadequately cooked. Pepper and Diaz (1945) state that the disease is so protean in its symptoms that the following conditions must be excluded: acute abdomen, nephritis, *typhoid fever, angioneurotic edema, polyneuritis,* asthma, myositis of other etiologies, tetanus, ophthalmia, German measles, scarlet fever, erythema multiforme, meningitis, encephalitis, myocarditis and periarteritis nodosa. *Occasionally the most characteristic symptom is a marked adenitis,* particularly of the parotid glands. Clinically the disease requires differentiation in its early stages from acute digestive upsets, cholera and dysentery. *Later typhoid must be ruled out.* Many of the milder cases may be suggestive of intestinal "flu," with aching rheumatic pains of the muscles. Reiman, Price and Herbut (194[illegible]
periarteritis nodosa associated with [illegible]
Moreover, there may be thrombi in the blood vessels of the viscera [illegible] extremities associated with hemorrhages from these vessels. Nephritis may [illegible] the absence of albumin in the urine. Trichinosis [illegible]
shou[illegible]
conj[illegible]
caus[illegible]
the [illegible]
the amount of eosinophilia is not necessarily an index of [illegible] infection (Gaase, 1944). The occasional recovery of the adults in the feces during the initial diarrhea or of the larvæ in the blood, *spinal fluid* or

mother's milk during the period of migration is specifically diagnostic. McNaught (1939) calls attention to the "splinter hemorrhages" which appear beneath the finger nails of patients during the stage when the larvæ are migrating from the intestinal wall to the musculature.

The removal by biopsy of a small piece of the deltoid, biceps or gastrocnemius muscle from the vicinity of its tendinous attachment and examination in a trichina press under low power of the microscope may reveal the presence of pre-encapsulated or encapsulated larvæ. Biopsied muscle strips, when digested in artificial gastric juice at 37° C. for several hours, provide a centrifugate which is both a more accurate and a more refined basis for diagnostic procedure than compressed muscle, using the trichinoscope. However, complement fixation is at times positive when small biopsied

fifteen days following exposure, the other involves the larva, appears about the thirtieth day and reaches its maximum intensity between the forty-fifth and sixtieth day. The intradermal test has proved to be of definite practical value, although Mazzotti and Lozano Hube (1944) obtained positives varying from 2.2 to 17.9 per cent in 1000 tests, depending

or

19:

subclinical) a small white swelling appears immediately around the injected site, surrounded by an unraised, irregular, erythematous area of about 5 cm. in diameter. Fading begins in 15 to 20 minutes. The test may be checked by a precipitin reaction. It should be noted that the intradermal reaction for trichinosis remains positive for years after an infection has been *acquired and does not necessarily indicate activity of the parasites. On the* other hand, the precipitin reaction is more sensitive in providing evidence of recently acquired trichinosis and is likely to become negative when the infection becomes quiescent. Roth (1945) has developed a simple slide precipitin test, using patients' serum and sterile living larvae digested out of infected muscle of laboratory animals. The test becomes positive ten *to twenty days after the first symptoms appear and is claimed to be more* sensitive and more trustworthy than the intradermal and precipitin reactions. Sussenguth and Kline (1944) recommend a slide flocculation test. (See Section VII on Technical Aids, pp. 604, 605, 607.)

Therapeusis.—There is no satisfactory treatment for terminating the disease before it runs its course. If trichinosis is suspected during the early

mucosa. After specific diagnosis has been made, palliative measures should be used and the patient made as comfortable as possible. Supportive treatment consists in keeping the bowels open and alkalinized, and in giving special attention to the kidneys, which must carry off most of the parasite's

toxins. Sedatives, such as sodium amytal, should be administered to reduce the muscular pain, and heart and respiratory stimulants may be needed. In dehydrated patients hypertonic saline infusions may be introduced by hypodermoclysis. Van Someren (1939) states that 5 cc. of calcium gluconate (10 per cent solution), administered intravenously during the period of larval migration, reduces the temperature and minimizes intestinal and muscular pain.

Special attention should be directed to myocardial lesions caused by migrating larvæ. While the larvæ do not normally become encapsulated in heart muscle, they provoke a cellular infiltration leading to fibrosis and permanent damage, with symptoms mimicking essential hypertensive myocarditis (Blumer, 1936).

Progr[illegible] good. [illegible] In Ma[illegible] for the decennium 1936–1945 there were 287 cases reported to the State Department of Health. Seven of these died as a result of the disease (Ober, 1946). If the patient can withstand the active periods of the disease, it gradually subsides and slow recovery is effected However, myocardial or cerebral damage resulting from migration of the larvæ may leave the patient a permanent invalid. The numerous microscopic cysts in the striated muscles appear to produce no appreciable lasting inconvenience to the host.

Control.—With the knowledge that the pig is the reservoir host of the infection, careful inspection of meats in the large slaughter houses in Europe reduced the epidemics of serious cases to a minimum, but there are undoubtedly hundreds of undiagnosed cases throughout the less populous endemic areas. [illegible] are ineffectual. [illegible] Ransom and other workers have shown that refrigeration at 5° F., (—15° C.) for not less than twenty days (Ransom, 1916), or at —0.4° F. (—18° C.) for twenty-four hours (Augustine, 1933), renders infected flesh practically innocuous. Boiling of trichinized meat for a period of one-half hour for every pound of flesh is a fool-proof method of sterilizing pork with respect to the infection. American pork products which are customarily eaten raw are properly prepared only in government-inspected slaughter houses; country-killed meat is not supervised (Schwartz, 1929).

In summarizing the present day rationale of control in the United States Gould (1945) has outlined six possible methods, namely (1) inspection of hogs, (2) education of the public, (3) destruction of rats, (4) cooking all garbage fed to hogs, (5) skin-testing of hogs to determine and condemn positives and (6) processing meat by heat or refrigeration Destruction of rats is not of major value. Inspection and testing of hogs is unreliable and provides a false sense of safety. Education of the consumer is desirable but not effective. Cooking of garbage is very valuable but difficult to enforce. Storage in deep-freeze units at 0 to 5° F. offers a modern method which is both simple and effective (providing the consumer can be persuaded to eat frozen rather than chilled pork).

In 1948 the Committee of Public Health Relations of the New York Academy of Medicine submitted a report (Pub. Health Repts, 63(15),

478–488) on control of trichinosis. After reviewing evidence in support of the conclusion that trichinosis is a serious public health problem in the United States, and weighing the relative merits of microscopic examination of pork, refrigeration and quick freezing and boiling of garbage, the Committee regards garbage treatment as the most practical but recommends that additional studies be initiated "to determine whether more effective measures for the destruction of trichinae in pork products can be devised without an undue increase in cost."

Family TRICHOCEPHALIDÆ Baird, 1853

The members of this family have a characteristic capillary anterior end. According to C. H. Li (1933) the anterior end of this worm is provided with a delicate, protrusile spear, suggesting a relationship to free-living forms, but Chitwood (1937) regards the spear, together with the muscular elements of the organ, as an adaptation to hemophagous habits. The male worms have a copulatory sheath and usually possess a copulatory spicule. The eggs are barrel-shaped and possess clear polar prominences. The life cycle of these species is direct, the worms requiring but one host. They live in the intestinal tract, liver or urinary bladder of mammals and birds.

GENUS TRICHOCEPHALUS SCHRANK, 1788. (Syn. TRICHURIS ROEDERER, 1761)

(genus from θρίξ, hair, and κεφαλή, head)

Trichocephalus trichiurus (Linnæus, 1771) Blanchard, 1895. (The human whipworm, producing trichocephaliasis, trichuriasis or whipworm infection.)

[Common synonym, *Trichuris trichiura* (Linn., 1771) Stiles, 1901.]

The generic name for the human whipworm is in dispute and has not been ruled on by the International Commission on Zoological Nomenclature. A special committee of The American Society of Parasitologists has reported (1941) in favor of *Trichuris* but convincing arguments have also been made in favor of *Trichocephalus*.

Synonyms.—*Ascaris trichiura* Linn., 1771, *Trichocephalus hominis* Schrank, 1788; *Trichuris hominis* (Schrank, 1788) Brugière, 1791; *Trichocephalus dispar* Rud., 1802, *Mastigodes hominis* (Schrank, 1788) Zeder, 1803; probably also *Trichocephalus suis* Schrank, 1788.

Historical and Geographical Data.—The human whipworm was first observed by Morganni towards the end of the seventeenth century, but this observation was forgotten and the worm was apparently not again observed until 1761, when Roederer studied specimens recovered from the cecum of an anatomical preparation made by one of his students in Gottingen. He discovered that the worm was new and proposed for it the name *Trichuris*, believing that the filiform end was the tail. Goeze (1782) corrected this error and renamed the worm *Trichocephalus*. Linnæus (1771) first provided it with a binomial, *Ascaris trichiura*. Schrank (1788) called it *Trichocephalus hominis*. Since neither Roederer nor Goeze abided by the rules of

This worm is cosmopolitan in distribution but is most prevalent in the warm, moist regions of the world. In the moist Tropics the incidence usually ranges from 50 to 100 per cent and the amount of the infection (*i. e., worm burden*) is correspondingly high. In Europe the following incidence percentages have been reported: Copenhagen, 28 (Roth); Basel, 11.7 . . .
Prague, 6.7 (Gabriel); E. Prussia, 84
infection is uncommon in the northern . .
United States it may be present in 20 to 25 per cent of populations surveyed but the worm burden is usually low. Stoll (1947) has estimated the world incidence at 355.1 millions, including 227 in Asia, 27.2 in the U. S. S R., 34 in Europe, 28 in Africa, 38 in tropical America, 0.4 in North America and 0.5 in the Pacific islands

Structure of the Adult Worm and The Life History.—The adult whipworm, *Trichocephalus trichiurus*, commonly lives in the human cecum, but it is frequently found in the appendix vermiformis, on occasions in the colon and rectum, and in the posterior part of the ileum. Man is the only commonly accepted host of this species, but the worm found in the pig and in certain monkeys (*Colobus ruformitratus* and *Cercopithecus diana*) may be the same species.

The male worm measures 30 to 45 mm. in length, the anterior three-fifths being a capillary tubule and the posterior two-fifths being more fleshy. The caudal extremity is coiled ventrad as much as 360 degrees or even more (Fig. 199 *A*). The male genitalia consist of (1) a sacculate testis, which ascends from the posterior end of the worm towards the anterior levels of the fleshy portion, (2) a vas deferens, which turns abruptly posteriad and descends to the cloacal region, and runs into (3) the ejaculatory tubule (cirral organ), before emptying into the cloaca. The single, lanceolate spicule, which measures 2.5 mm. in length, protrudes through the retractile sheath at the posterior extremity of the body. The sheath has a bulbous end and is beset with numerous recurved spines, which serve to hold the male in coitus at the time of copulation.

The female worm (Fig. 199 *B*) measures from 35 to 50 mm. in length, is bluntly rounded at the posterior end, and has approximately the same proportions of capillary and fleshy parts as the male. The vulvar opening is situated ventrally at the anterior extremity of the fleshy portion. The ovarian tubule arises as a sacculate organ near the posterior end of the body and proceeds anteriad to the middle plane of the fleshy portion, after which it merges with the oviduct, which, in turn, descends in a tortuous track to the subcaudal plane. After partial coiling, it runs forwards for a short distance, to join the large uterine pouch, which ascends through the fleshy portion of the body and, some little distance behind the vulva, constricts into a serpentine tubule, which proceeds to the external pore. The worm is oviparous, the eggs when extruded containing a single blastomere.

The eggs are barrel-shaped, possess an outer and an inner shell and have transparent polar prominences. (Fig. 199 *C*). They measure 50 to 54 μ in length by . . . Leuckart (1876) estimated that each
female lays . .
Manalang . . .
and Correa and Mellone (1938), 315 eggs *per* gram of formed .

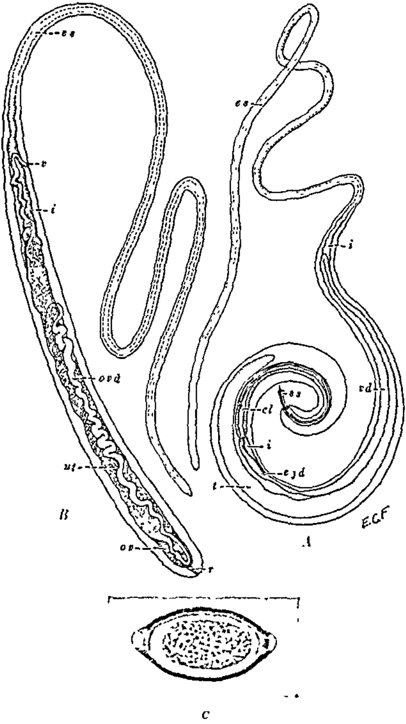


FIG. 109. *Trichocephalus trichiurus*. *A*, male worm, × 12. *B*, female worm, × 12. *C*, photomicrograph of egg, × 666. *cl*, cloaca, *ejd*, ejaculatory duct, *es*, esophagus, *i*, midgut; *ov*, ovary, *ovd*, oviduct, *ss*, copulatory spicule and sheath, *t*, testis, *ut*, uterus, *v*, vulva, *vd*, vas deferens. (*A*, *B*, originals, from dissections of specimens obtained from man at autopsy, *C*, after Faust, in Brennemann's Practice of Pediatrics, courtesy of W. F. Prior Company.)

ever, the latter two estimates were calculated from egg-counts made *post-mortem* on colonic feces and are therefore probably not true indices of egg production. Miller's study (1939) of egg production for *T. vulpis* in six dogs showed a daily range of 1349 to 4808 eggs per female worm, varying inversely with the number of worms infecting the dog (average, 2035 eggs). The first division of the egg is transverse but unequal. The second is also transverse, being a division of only the blastomere at the vegetal pole. The third division is a longitudinal division of the medial cell. Thus the four-cell stage is the result of three rather than two segmentation stages. Development of the first-stage larva within the egg takes place outside the body of the host. The time required for this development depends on the type of environment, but requires 21 days or more (Brown, 1927), although Miller (1939) has reported an embryonation period as short as nine or ten days for the dog whipworm (*T. vulpis*). Apparently no larval ecdysis occurs within the unhatched egg. Extremely dry conditions prevent embryonation. Spindler (1929) demonstrated that moisture is much more essential for the development of this egg than had previously been supposed. Human beings become infected as a result of swallowing the fully embryonated eggs contaminating food or drink.

The various steps in the life cycle, as first described by Grassi (1887) on the human whipworm, and more recently by Fulleborn (1923) for whipworms of monkeys and rabbits and Hasegawa (1924) and Miller (1939) for the whipworm of the dog, indicate that the egg-shell is weakened by the intestinal juices and the activated, weakly muscular larva breaks out of the shell. It soon invades the glandular crypts and penetrates into the glands and stroma, in which it becomes coiled, meanwhile causing considerable [illegible] cellular reaction. For a period of about ten days these [illegible] in the region of the cecum and appendix. There is no [illegible] indicating that a migration to the lungs is required or utilized. Approximately three months are required for the complete development from exposure until egg-laying begins.

Epidemiology.—As Cort and his associates have shown (1926–1938), the human whipworm's distribution is usually coextensive with that of *Ascaris lumbricoides*, but there are areas of heavy rainfall, high humidity and densely shaded, moist ground where the whipworm is much more prevalent, and, on the other hand, other areas with less rainfall and shade, where ascariasis is more prevalent. Regions with high incidence and heavy whipworm burden are usually those polluted by children of school age (5 to 13 years of age), who are more usually infected than the adult population. Infection results directly from ingestion of fully embryonated eggs picked up from the soil or contaminating food or drink.

Once established in the human bowel, the whipworm may live for many years.

Pathogenesis, Pathology and Symptomatology.—Much has been written about the pathogenicity of the human whipworm but very few facts are known. In tropical and Oriental countries the infection is common, worms being present in the cecum in 25 or more per cent of the population. No

appreciable clinical symptoms are usually elicited from persons harboring light infections. However, Caldwell and Caldwell (1929) state that cases occur in which symptoms are pronounced and that the degree of symptoms is not necessarily correlated with the number of worms present, although, by and large, heavy worm burdens produce more demonstrable symptoms.

The worms are attached by their anterior ends to the mucosa, or are sewed into the mucosa, and a film of mucus usually surrounds the oral end. According to Hoeppli (1930), the worm secretes juices which liquefy the cells of the intestinal mucosa adjacent to the attached end. Guiart (1908), Brown (1934) and Chitwood (1937) believe that the worm may suck blood. However, there is ordinarily no considerable tissue reaction and the adjustment of host tissue to parasite may be said to be that of nearly balanced equilibrium. Occasionally the head of the worm extends through to the submucosa or the muscularis and on rare occasions it may possibly perforate through to the body cavity. Under such circumstances a more or less serious inflammatory reaction may result. If the worms lodge in the lumen of the appendix they may cause occlusion of this organ, or may suck sufficient blood and produce sufficient inflammation to produce an "acute appendix." The majority of the worms are concentrated in the cecum and appendx but in heavy infections they may be basted into the mucosa of the ascending colon or even extend down to the anus. Relatively few are attached to the lower portion of the ileum.

In a study of an Italian ship's crew during 1942–1943, 81 members were found to be infected with *T. trichiurus.* The associated symptoms reported (expressed in per cent) in the order of frequency were: pain over McBurney's point, 37; chronic constipation, 37; periodic abdominal distress, 34; gaseous eructations, 30; neurotoxic manifestations, 30; vertigo, 30; indigestion, 28; loss of weight, 25; pruritus, 18; burning sensation in the abdomen, 16; nausea and/or vomiting, 15. Twenty-one per cent were symptomless (Plessen, 1945).

During the period 1941–1944, 50 children with uncomplicated whipworm infection were studied clinically in the Gorgas Hospital, Canal Zone. About half of these patients came from rural areas and the other half from principal cities in Panamá. The majority had a severe infection. The average history indicated a diarrhea of from one to three months' duration as the most significant manifestation of the acute stage. Frequently the stools were blood-streaked and there were abdominal pain, tenesmus and progressive loss of weight. Chronic infection was frequently responsible for repeated prolapse of the rectum, with worms visible, sewed into the rectal mucosa. Petechial hemorrhages occurred at the sites of attachment when attempts were made to remove the worms by traction (Whittier, Einhorn and Miller, 1945).

In some individuals, particularly children, signs and symptoms, consisting of loss of appetite and loss of weight, edema of the face and hands, dyspnea, cardiac dilatation, hepatitis, a secondary anemia with a disproportionately reduced hemoglobin (*i. e.,* 2,300,000 rbc with 30 per cent Hb in children with 400 to 4100 worms at necropsy, *fide* Getz, 1945), eosinophilia occasionally up to 25 per cent, insomnia, sympathetic neuroses, and even epileptiform seizures, rarely an urticaria, are produced.

Perhaps the most serious rôle played by *Trichocephalus trichiurus* is the opportunity which the worm offers for secondary invaders, as staphylococci and streptococci, to enter the puncture wounds made by the worms, and to produce submucosal abscesses, which break through to the surface as multiple ulcers. They are particularly found in the cecum and ascending colon. At times vascular thrombosis may develop in the adjacent deeper layers of the bowel wall (Garin, 1911).

Diagnosis.—Based on the recovery of the characteristic eggs in the feces of the patient. Manalang (1928) has estimated that each female worm averages 150 eggs *per* gram of formed feces, but there is evidence that egg-laying in the whipworm is much less constant than in the hookworm and hence less dependable as a means of estimating the number of worms present in an infection. Correa and Mellone (1938) made egg counts in 19 whipworm-infected autopsies and obtained an average of 315 eggs *per* female *per* gram of feces, or 200 eggs *per* gram of feces for both females and males recovered.

Therapeusis.—None of the available drugs which are efficient for the removal of hookworms, *Ascaris lumbricoides*, *Enterobius vermicularis* or *Strongyloides stercoralis* are particularly satisfactory for use in whipworm infections. It is true that full therapeutic doses of oil of chenopodium dislodge the majority of whipworms in a heavily infected patient, but this drug is very toxic and should not be administered in the amount necessary to eradicate the worms. Likewise, Pallister (1933) obtained a heavy yield of evacuated worms after administering 8 cc. of carbon tetrachloride with 2 cc. of oil of chenopodium. However, these dosages are considerably in excess of the normal tolerance of patients and are not recommended for the average case. For patients harboring a large number of these worms it is safer to administer several weekly doses of tetrachlorethylene in amounts of 3 cc. for each administration (adult dose) or 3 minims *per* year of age (children's dose)

In the event that tetrachlorethylene, carbon tetrachloride, oil of chenopodium, or a combination of either of the first two in the amount of 2.7 cc. with 0.3 cc. of oil of chenopodium is prescribed, it is essential that the bowel be evacuated of feces before specific therapy is instituted High enemas, followed by purgation with Glauber salts (sodium sulfate), 15 Gm or one-half ounce in a glass of water, taken the night before treatment, will not only clean out the bowel, particularly removing the viscous feces surrounding the worms in the cecal area, but will also remove mucus from the heads of the worms. Within two hours after specific therapeusis has been carried out saline purgation should be repeated, to safeguard the patient against excess absorption of the drug (in the case of carbon tetrachloride and oil of chenopodium), as well as the toxic by-products of dying worms.

The above recommendations are not likely to be effective in removing a small number of whipworms.

A specific anthelmintic for whipworms, known at least since 1770 (Bajon) is the crude latex of the fig tree, *Ficus glabrata* (syn. *F. laurifolia*) of Central America and Northern South America, and its relative, *F. doliaria*, of Brazil. The fresh latex (*leche de higuerón*) is taken on an empty stomach in

2-ounce (60 cc.) doses, usually without pre-treatment or post-treatment purgation. No ill-effects from its administration have been noted. Unfortunately this latex rapidly ferments unless kept on ice. Caldwell and Caldwell (1929) found that the therapeutic dose produced an 85 per cent egg reduction in their series of treated cases, with cures in 54 per cent of their patients, while oil of chenopodium, administered to an equal number of cases, produced only 17 per cent egg reduction and 1.7 per cent cures. A proprietary preparation of the crude latex from Colombia, preserved in one per cent sodium benzoate and marketed under the name "Higueroma," is available in parts of Latin America. The present author has found that its efficiency is not more than 75 per cent that of the fresh, unpreserved, refrigerated latex. The effective fraction of *leche de higuerón* is ficin, a proteolytic enzyme recovered by Robbins (1930). As yet it has not been adequately tested to guarantee its practical efficiency or safety.

Burrows, Moorehouse and Freed (1947) obtained about 88 per cent worm removal in 23 adult patients in a mental hospital. Eleven of these individuals lost all of their worms. This followed administration of emetine hydrochloride in Enseals (Lilly) coated tablets of 0.02 Gm. size, with a dosage ranging from 3 tablets a day for twelve days to 16 tablets in one period of 24 hours. The drug produced considerable diarrhea and dysentery, nausea and vomiting.

Prognosis.—Good to fair in untreated, lightly infected cases; fair to poor in untreated, heavily infected persons showing effects of the infection. When a satisfactory anthelmintic is available, the prognosis will be excellent.

Control.—This consists in the sanitary disposal of human feces, particularly in moist, warm countries, where rural sanitation is most needed. Thorough cleansing of the hands before meals should reduce human infection. Children, in particular, must be taught to use sanitary toilets and to keep their hands out of their mouths when playing on the ground. When an available specific anthelmintic is found, an additional weapon for controlling this infection will be provided.

Related Species.—Many closely related species of *Trichocephalus* are found in other mammals, including *T. campanulus* and *T. serratus* in the cat, *T. discolor* in the cow, *T. leporis* in the rabbit, *T. muris* in rats and mice, *T. ovis* in sheep and goats, *T. suis* in the pig, and *T. vulpis* in the dog and fox.

Genus Capillaria Zeder, 1800

(genus from *capillus*, hair)

Capillaria hepatica (Bancroft, 1893) Travassos, 1915. (The capillary liver worm.)

Synonyms.—*Trichocephalus hepaticus* Bancroft, 1893, *Hepaticola hepatica* (Bancroft, 1893) Hall, 1916.

Biological and Epidemiological Data.—*Capillaria hepatica* is a trichocephalid nematode living in the liver tissues of the Alexandrine rat, the black rat, the brown

monkey (*Cebus capucinus imitator*). One authentic case has been recorded from a man, a British soldier in India, and a second true hepatic infection in man has more recently been diagnosed in the Charity Hospital of New Orleans, La. (1948). Skrjabin *et al.* (1929), Blackie (1932), Vogel (1932), Sandground (1933), Faust and Martinez (1935), Wright (1938), J. F. Crow (personal communication, 1947) and Brosius, Thomas and Brosius (1948, Trans. R. Soc. Trop. Med. and Hyg., 42(1), 95–97) have recovered eggs of this species in the feces of patients who had either eaten the livers of infected animals or had exposed themselves to contaminations of disintegrating, infected livers. In none of these cases of spurious parasitism has there been any evidence of actual human infection. Foster and Johnson (1939) suggest that the presence of *Capillaria* eggs in feces of Panamanians is probably due to eating the cooked, infected livers of the peccary and local monkeys. The worm also develops normally in the dog and the chimpanzee. Natural infections in reservoir hosts have been recorded from America, Europe, Australia and India; rats and mice are not infrequently infected in China and Japan.

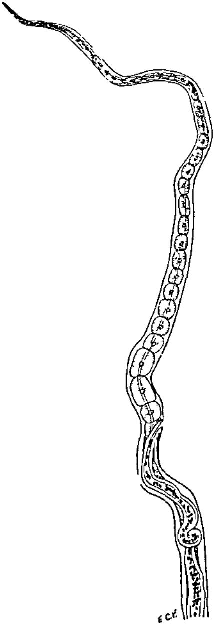


Fig. 200.—*Capillaria hepatica;* anterior end of female worm, showing capillary esophagus and vulva × 16. (After Nishigori.)

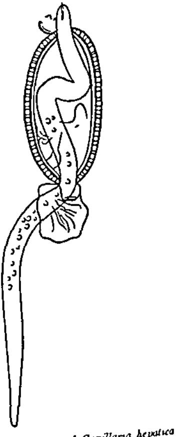


Fig. 201.—Larva of *Capillaria hepatica* emerging from egg-shell. Highly magnified (After Fülleborn, Archiv für Schiffs- und Tropen-Hygiene.)

When dissect

Trichocephalus,

is proportionally shorter than that of *Trichocephalus*

spicule is only slightly chitinized and tapers to a fine point. It is enclosed in a protrusile membranous she
the esophageal region.
characteristic pattern fo
perforated with minute
The eggs of the related species, *C soricicola* Nishigori, 1924, are longer and more slender.

The life cycle of this species, like that of *Trichocephalus*, is direct, requiring only a single host. According to Nishigori, the eggs are deposited in the parenchyma of the liver and are not excreted. Less than a month after they are laid they contain mature embryonated larvæ. These are transferred to the next host when the infected organ is eaten by that host, or through the natural decomposition and disintegration of the viscera of infected hosts and subsequent contamination of the food or drink

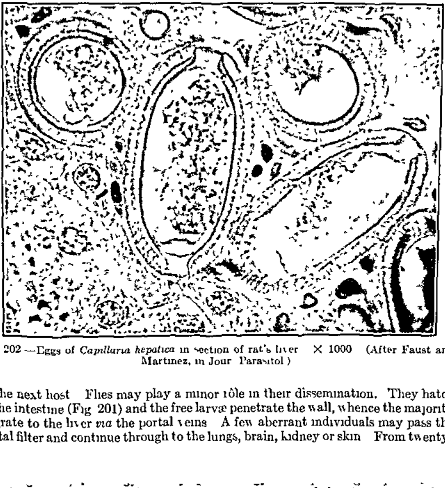


FIG 202 —Eggs of *Capillaria hepatica* in section of rat's liver × 1000 (After Faust and Martinez, in Jour Parasitol)

of the next host Flies may play a minor rôle in their dissemination. They hatch in the intestine (Fig 201) and the free larvæ penetrate the wall, whence the majority migrate to the liver *via* the portal veins A few aberrant individuals may pass the portal filter and continue through to the lungs, brain, kidney or skin From twenty-

sists in the formation of fibrous connective tissue around depots of eggs and in light infections involves only a localized area In heavy infections, however, the liver of the rodent host may be affected by a generalized cirrhosis Here the eggs may be destroyed by giant cells or may remain for as long as two years Toxic symptoms, consisting of a diarrhea, dyspnea and congestion of the liver, may result from heavy infections In the first human infection on record, reported by Mac-

Arthur from material furnished by Dive, the symptoms were said to resemble pyemia, and *postmortem* examination revealed a suppurative condition of the liver with spongy areas, which, under the microscope, revealed the presence of large masses of *Capillaria hepatica* eggs.

Diagnosis.—Possible only at *postmortem*, by examining scrapings of the infected organs or by sectioning the tissue and finding the characteristic eggs. In genuine infections the eggs are not discharged in the urine, the bile or the feces.

Therapeusis.—Unknown.

Prognosis.—Probably poor.

Control.—Infection among rodents is doubtless due to cannibalism, or to ingestion of naturally decomposed viscera of infected hosts (Tubangui, 1931). Due to the source of infection, human cases are bound to be rare. Human food and drink should be protected from contaminations. Care must be exercised not to confuse spurious with genuine infections.

Superfamily Mermithoidea Wülker, 1924

This group consists of several genera grouped under the families **Mermithidæ** Braun, 1883, and **Tetradonematidæ** Wulker, 1934.

The adult Mermithidæ are readily visible to the naked eye and some reach the length of 10 to 20 cm or more. They are opaque objects, with a pointed anterior end, a tapering body and smooth, finely striated cuticle. Behind the non-muscular esophagus the intestine, if present, is modified into a *trophosome,* or storage organ for food, and in some species is completely lacking for a part of the way According to Steiner (1933), this is probably an adaptation to the parasitic life of mermithid worms in the body cavity of their arthropod host, which is richly supplied with predigested foods. In some species, however, a complete digestive tract is present in an early larval stage

In females the anal opening is represented by a slight indentation of the cuticle: in males the cloaca persists to permit an outlet for the spermatozoa, but the intestine

for the larval stage is *Agamomermis.*

Two cases of human infection with larval mermithids are recorded by Stiles and Hassall (1926), both of which were originally described by Leidy. The former, *Agamomermis hominis oris* (Leidy, 1850), was about 14 cm. in length and was obtained from the mouth of a child. The second, *Agamomermis restiformis* (Leidy, 1880), was 65 cm long and 1 5 mm. in diameter and was recovered while attempting to emerge from the penial opening of an adult white man.

A third case of infection with a mermithid worm has been reported by Baylis (1927). The worm is said to have been passed by a woman thought to be suffering from uterine cancer. The specimen (alcoholic preservation) was of a pinkish flesh color, totaling about 56 cm. in length and having a maximum breadth of a little less than 1 mm was a

An

due to

The presence of mermithids in the human body is undoubtedly accidental, due to ingestion of the worms in food, water or moist earth into which the worms have found their way after migration from the invertebrate host, or due to swallowing the invertebrate host with its parasitic progeny.

Suborder Dioctophymatina (Skrjabin, 1923) Pearse, 1936

(Syns. Dioctophymida Sprehn, 1927; Dioctophymeata Petrov, 1930, Dioctophymata Skrjabin, 1923)

Members of this large division of the enoplid Aphasmidia (of Chitwood and Chitwood, 1933) are lipless species which have a rudimentary mouth, with or without cephalic suckers. They have a well-developed, cylindrical esophagus and an intestine. The amphids are labial in position and pore-like. Caudal glands are lacking. The sexes are monogonic. The male is provided with a single spicule, lacks a gubernaculum and has a muscular, suctorial bursa, unsupported by rays, at its caudal extremity. The female has a long, muscular vagina and is oviparous. The eggs have thickened, pitted shells, which are lighter at the poles. The described species all belong to the superfamily **Dioctophymatoidea Railliet, 1916,** and to the type family **Dioctophymatidæ Railliet,** 1915. Of the four recognized genera of this family, one species, *Dioctophyma renale*, has been reported as a human parasite.

Genus Dioctophyma Collet-Meygret, 1802

(genus from διογκόω, to swell, and φῦμα, tubercle)

Dioctophyma renale (Goeze, 1782) Stiles, 1901. (The giant kidney worm.)

Synonyms.—*Ascaris renalis* Goeze, 1782; *Ascaris canis et martis* Schrank, 1788;

including the dog, wolf, *Canis jubatus*, puma, glutton, raccoon, coati, marten, skunk, weasel, mink, otter, seal, ox and horse It has been reported from Europe, North and South America, and has been obtained once in China (Nanking) and once in Brazil (Lisbôa, 1945) It has been found as a human parasite more than nine times (Brumpt).

Morphology, Biology and Life Cycle.—The worm is reddish in color, cylindrical in shape, slightly attenuated at both ends, and measures 14 to 20 cm in length by 4 to 6 mm. in diameter for male specimens (Fig. 203 *A*) and 20 to 100 cm. in length by 5 to 12 mm. in diameter for females. Along the lateral line of each side there is a series of punctate papillæ The hexagonal mouth (Fig 203 *B*) is provided with two series of well-developed, nodular papillæ, six in each series, two pairs of which correspond with the commencement of the two lateral "lines." Surrounding the caudal extremity of the male worm is a bursal cup (Fig. 203 *C*), the margin of which, as well as the inner depth, is provided with very minute papillæ The cloacal opening is near the center of the bursal pocket The single setiform, copulatory spicule measures 5 to 6 mm. in length. The vulva of the female is situated 5 to 7 cm from the anterior end of the worm.

The eggs (Fig. 203 *D*, *E*) are ellipsoidal, brownish-yellow in color, and have a thick shell with sculptured depressions on all parts of the surface except the poles. They measure 64 to 68 μ in length by 40 to 44 μ in transverse diameter. According to the observations of Balbiani (1870) the eggs begin to segment at the time of oviposition. Complete develop-

ment of the larva *in ovo* requires six months or less, depending on the season. The eggs are extremely resistant to external conditions and may remain viable for five years or more.

The first stage larva is fusiform, measuring about 240 by 14 μ. In the

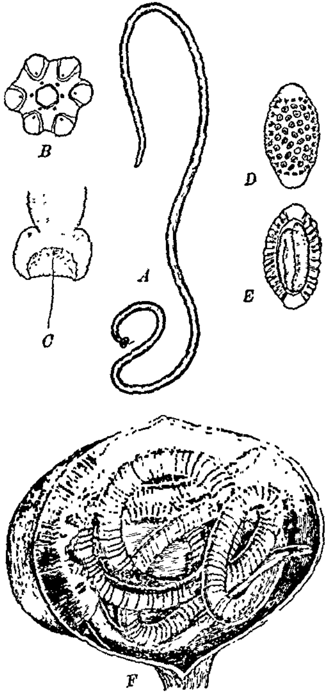


Fig. 203.—*Dioctophyma renale.* A, ac
Ra
sho
mu
F,
three-fourths natural size. (After Railliet,
Frères, Paris.)

anterior part of its esophagus there is a three-toothed onchium The *life cycle* lacks complete elucidation. Ciurea (1921), following Leuckart's clue, has been able to infect one of a litter of four puppies by feeding raw fish (*Idus idus*) containing encysted mature larvæ. Woodhead (1945) has found experimentally that after six months' incubation the larvæ within the eggs are infective for branchiobdellid annelids which are semi-parasitic on crayfishes. On ingestion by these worms the eggs hatch and in about ten minutes penetrate into the body cavity of the worms. About ten days are required for the larvæ to metamorphose into second-stage, gordius-like larvæ When the bronchiobdellids are eaten by the Northern black bullhead (*Ameiurus melas melas*), the larvæ excyst, migrate to the mesenteries of the fish and re-encyst Like gordiid worms in crickets, the larvæ now [illegible]

[illegible] ost becomes infected. Woodhead [illegible] n egg to adult requires two years. [illegible] . *Man and other mammals acquire* infection from consuming infected fresh-water fish, raw or inadequately cooked, containing the infective (third) larval stage of the worm.

Pathogenesis, Pathology and Symptomatology.—The adult worms live in *the pelvis of the kidney or in the body cavity. One or more worms may be* present at one time, the largest number recorded being eight from the kidney of a wolf In the kidney they little by little consume the renal parenchyma (Fig. 203 *F*), finally leaving only the enveloping tunica. The urine in these cases contains blood and pus. Renal colic and other direct symptoms result during the early stages, while in late cases dysfunction of the infected organ is complete. In infected dogs several types of nervous disorders have been ascribed to the presence of the worms, including rabid symptoms The worms may attempt to escape down the ureter and produce acute uremic poisoning or may succeed in escaping from the urethra. The Brazilian case, the tenth human case to be reported, was a fifty-four-year-old white resident of Maranhão Province. She had a history of pruritus vulvæ. One day during micturition the urethra became temporarily occluded. Following straining a large roundworm was passed, terminating the pruritus. The worm proved to be a mature male *D. renale* (Lisbôa, 1945). All of the authenticated human cases have had renal infections, but the worm has been recovered from the abdominal and thoracic *cavities and from the liver of dogs.*

Diagnosis.—In renal infections, where a female worm is present, the discovery of the typical eggs in centrifugalized or sedimented urine is diagnostic

Prognosis.—*Usually very grave.*

Therapeusis.—The only known method of removing the worm is by operation, although it may be passed spontaneously *per urethram*

Control.—Thorough cooking of fresh-water fish, if the latter is the normal *intermediate host, will remove the possibility of individual danger.*

CHAPTER XXV.

THE PHASMID NEMATODE PARASITES OF MAN

Subclass Phasmidia Chitwood and Chitwood, 1933

ORDER RHABDITIDA CHITWOOD, 1933

This order contains great assemblages of free-living and parasitic species. Among them are some of the most important helminth parasites of man. They are all characte[illegible] a triradiate lumen. [illegible] in four suborders, each having one or more superfamilies, which, in turn, are represented by one or more families. These families with their respective species will be taken up *ad seriatim* according to the classification presented in Chapter XXIII (pp. 353–355).

Suborder Rhabditina (Chitwood, 1933) Pearse, 1936

Superfamily Rhabditoidea Travassos, 1920

(Strongyloides and Related Forms)

From a structural viewpoint the members of this group are relatively simple forms. Biologically many of them are on the borderline between a free-living and a parasitic condition. For some, the mode of existence is facultative; for others, environmental factors appear to be the determining element as to whether the worm at any particular time is free-living or parasitic The species recorded from man are grouped under the families **Rhabditidæ** and **Strongyloididæ**.

Family RHABDITIDÆ Micoletzky, 1922

This family contains species which previous authors have usually placed under the **Rhabdiasidæ, Anguillulidæ** or **Angiostomatidæ**. More recent studies [illegible] fundamental characters of the present [illegible]

[illegible] bulbar swelling. The species which have been [illegible] to the genera *Rhabditis* and *Turbatrix*. All species are normally saprozoic.

Genus Rhabditis Dujardin, 1845

(genus from ῥάβδος, a small rod)

Rhabditis pellio (Schneider, 1866) Buetschli, 1873.

[illegible] *[illegible]llula mucronata* Grube, 1849; [illegible]

thickening. The esophagus is slightly swollen anteriorly and enlarges posteriorly into a bulbus provided with teeth.

The male measures 0 99 to 1 81 mm. in length. The caudal extremity is provided with

spicul

cauda

cavity of the mother worm, many containing all of the organs of the mother so

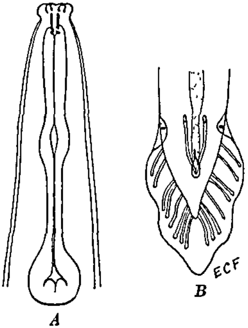


FIG 204 —*Rhabditis pellio*, *A*, anterior end of worm, showing buccal cavity and esophagus, *B*, posterior end of male, showing spicules, bursa and bursal rays × ca 350 (After Oerley.)

that the larvæ finally appear to lie in a spindle-shaped sac consisting of the intact cuticle of the parent worm. Together with functional males and one-sexed females, Johnson (1913) found hermaphroditic females in fluctuating numbers. The complete life cycle of this worm has not yet been elucidated.

Scheiber (1880) found these worms in the urine of a female patient suffering from pyelonephritis, pneumonia and acute intestinal catarrh The urine was acid and contained albumin, pus and blood The adult worms were situated in the vagina and the larvæ were evacuated with the urine The worms reported by Boginsky (1887) and by Peiper and Westphal (1888) from patients with similar histories probably belong to this species Aubertot (1923) has shown that *R. pellio* may pass uninjured through the alimentary tract of the fly *Drosophila*. Oerley (1886) has found that the worm will live in the vagina of a mouse. The fact that the Hungarian

CHAPTER XXV.

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ORDER RHABDITIDA CHITWOOD, 1933

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Suborder Rhabditina (Chitwood, 1933) Pearse, 1936

SUPERFAMILY RHABDITOIDEA TRAVASSOS, 1920

(STRONGYLOIDES AND RELATED FORMS)

From a structural viewpoint the members of this group are relatively simple forms Biologically many of them are on the borderline between a free-living and a parasitic condition. For some, the mode of existence is facultative, for others, environmental factors appear to be the determining element as to whether the worm at any particular time is free-living or parasitic. The species recorded from man are grouped under the families **Rhabditidæ** and **Strongyloididæ**.

Family RHABDITIDÆ Micoletzky, 1922

This family contains species which previous authors have usually placed under the **Rhabdiasidæ**, **Anguillulidæ** or **Angiostomatidæ**. More recent studies have served to demonstrate the fundamental characters of the present family grouping, consisting of a short prismatic or tubular buccal cavity, and an esophagus having a medium bulbar swelling and a posterior valvate bulbar swelling. The species which have been recorded from man belong to the genera *Rhabditis* and *Turbatrix*. All species are normally saprozoic.

GENUS RHABDITIS DUJARDIN, 1845

(genus from ῥάβδος, a small rod)

Rhabditis pellio (Schneider, 1866) Buetschli, 1873.

Synonyms.—*Pelodera pellio* Schneider, 1866; *Anguillula mucronata* Grube, 1849; *Angiostoma limacis* Dujardin, 1845 of Lieberkuhn, 1858; *Rhabditis genitalis* Scheiber, 1880; *Leptodera pellio* (Schneider, 1866) Ward, 1903

worms; as an adult it lives normally in decomposing organic matter in the soil (Roffredi) The adult worms have a smooth cuticle Their oral ends (Fig 204 *A*)

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y

The male measures 0 99 to 1 81 mm. in length. The caudal extremity is provided

the organs of the mother so

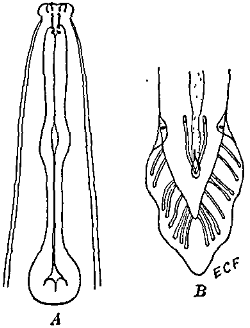

Fig 204 —*Rhabditis pellio; A*, anterior end of worm, showing buccal cavity and esophagus, *B*, posterior end of male, showing spicules, bursa and bursal rays × ca 350 (After Oerley.)

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Drosophila. Oerley (1886) has

The fact that the Hungarian

peasants use soil to make poultices would afford an opportunity for the worms to reach the vaginæ of women using such an application.

Rhabditis niellyi (Blanchard, 1885).

Synonyms.—*Anguillula leptodera* Nielly, 1882; *Leptodera niellyi* (Blanchard, 1885) Bl., 1890.

The des
Nielly anc
vicinity of
the skin resembling "craw-craw" of West Africa. In each papule there were found one or more larvæ. These larvæ measured 0 33 mm. in length by 13 μ in diameter, were attenuate anteriorly and posteriorly, and had fine transverse striations on the cuticle. The mouth opened into a short pharynx, which was succeeded by an esophagus having two bulbs, of which the posterior was provided with teeth. The anal opening was situated a short distance from the posterior end.

The origin of these larvæ and the method by which they gained entrance to the skin is obscure. It seems most probable, however, that they are facultatively saprozoic or parasitic, that they gained entrance through the skin, and like *Gnathostoma* in creeping disease in man, were unable to reach a location where they could proceed with their development.

Rhabditis hominis Kobayashi, 1914.

Synonyms.—*Rhabditis fæcalis* Watanabe, 1922.

Historical, Geographical and Biological Data.—This species of rhabditid worm was described and named by Kobayashi (1914) from fresh fecal specimens of Japanese school children. It has more recently been reported from the Southern United States by Sandground (1925) who has studied it in considerable detail. Possibly the worm obtained by Frese (1907) by lavage of the human stomach is also the same species. It seems likely that this nematode is more widely distributed than the records indicate and that it is confused with the free-living stages of *Strongyloides stercoralis*. (See Table 2.)

The adult worm (Fig. 205*A*) is cylindrical in shape with anterior and posterior attenuations, and possesses a find transverse striation of the cuticula. The buccal opening is provided with four labia; the cavity (*bc*) is cylindrical and measures 20 to 40 μ in length. The esophagus has a length of 0.17 to 0.2 mm. and consists of four parts (Fig. 205*B*), an elongate muscular tube, followed by an anterior bulbus, a short median tubular portion, and finally a posterior cardiac bulbus. The intestine originates at the posterior end of the esophagus and continues to the subcaudal region of the body where it narrows and joins the short rectum The latter opens through the anal pore in the female and into the cloaca in the male.

The male measures 0.9 to 1.2 mm. in length by 30 to 50 μ in diameter. The caudal alæ are rather narrow bands surrounding the cloacal opening (Fig. 205 *C*). Each half is supported by six short ribs (*bp*). The two spicules (*s*) are equal; each has a knob-like head and a sharp point. A small gubernaculum (*g*) is situated mesad just within the cloaca. Mid-ventral in position some little distance anterior to the cloacal opening are an inconspicuous anterior and posterior papilla

The female measures 1.5 to 2.0 mm. in length by 0.12 mm in diameter. The posterior end of the body is drawn out into a sharp point. The vulva is located in the middle of the body. The uteri are divergent. In young specimens each uterus is filled with 10 to 50 eggs, which are ellipsoidal in shape and measure 44 by 28 μ, but the older worms are filled with rhabditiform larvæ which have already hatched. The youngest larvæ which

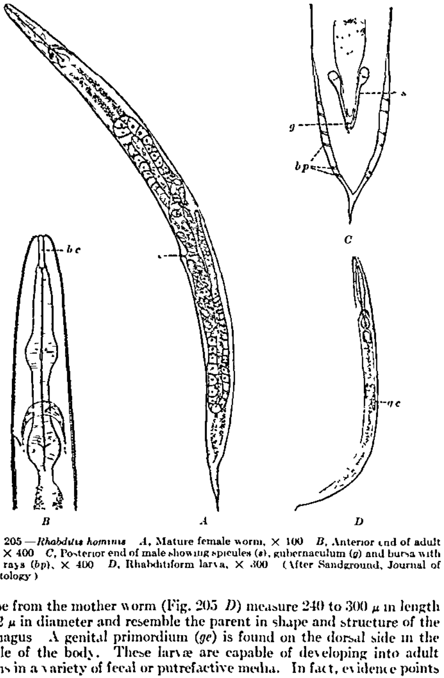

FIG 205—*Rhabditis hominis* A, Mature female worm, × 100 B, Anterior end of adult worm, × 400 C, Posterior end of male showing spicules (*s*), gubernaculum (*g*) and bursa with bursal rays (*bp*), × 400 D, Rhabditiform larva, × 300 (After Sandground, Journal of Parasitology)

escape from the mother worm (Fig. 205 *D*) measure 240 to 300 μ in length by 12 μ in diameter and resemble the parent in shape and structure of the esophagus A genital primordium (*gc*) is found on the dorsal side in the middle of the body. These larvæ are capable of developing into adult worms in a variety of fecal or putrefactive media. In fact, evidence points

TABLE. 2 —DIFFERENTIAL CHARACTERS OF RHABDITIS HOMINIS AND THE FREE-LIVING PHASES OF STRONGYLOIDES STERCORALIS

Rhabditis hominis	*Strongyloides stercoralis*
Male.	Male.
Dimensions. 0 9 to 1.3 mm. long; 0 03 to 0 05 mm. broad	*Dimensions: 0 7 to 0 9 mm long; 0 35 to 0 04 mm. broad.*
Buccal cavity: 20 μ long.	Buccal cavity. 13 μ long.
Bursa copulatrix· present, although often inconspicuous.	*Bursa copulatrix: absent*
Female	Female
Dimensions: 1.4 to 2 mm. long; 0 12 mm broad.	*Dimensions: 1 to 1 2 mm. long; 0 05* mm. broad
Buccal cavity· same as in male	
Reproduction: ovoviviparous.	
Eggs· 24 to 44 μ by 32 to 28 μ; often arranged in a double row in each *uterus; 20 to 50 in number.*	
Larva (young rhabditiform).	
Dimensions· 0 24 to 0.3 mm. long; 0 12 to 0 03 mm. broad.	0 016 mm broad.
Buccal cavity. 15 to 19 μ long	Buccal cavity: 8 to 10 μ long.
Genital primordium: 22 to 24 μ long.	Genital primordium. 34 to 36 μ long
This larva always develops into a rhabditiform sexual adult.	Tl

to the belief that the species is normally free-living and gains entry entirely by accident to the digestive tract of man, where it may remain for a time but where it never becomes a true resident. Contributory to this point of view is the fact that patients harboring the worms are not affected in the least by their

medication.

that the geographical distribution of the infection is probably similar to that of *Strongyloides stercoralis*, and that the larvæ of these two species may be readily confused The differential diagnosis of the two species (Table 2) is adapted from Sandground (1925).

Other species of *Rhabditis* reported from human feces include: *R. donbass* and *R. schactiella*, by Skrjabin, Schulz, Sserbinoff and Smirnoff, 1929, and *R. gracilis*, by Schingarewa, Demidowa and Kudriawzew, 1928.

There is no evidence that any of these species are genuine parasites, although Chitwood (1932) has shown that under favorable conditions *Rhabditis strongyloides*, and possibly other members of the group, may establish themselves in cutaneous ulcers of dogs, as those produced by bacteria, fungi and mange mites.

GENUS TURBATRIX PETERS, 1927

(genus

origin

Doctor T. Goodey, 1941.

Turbatrix aceti (Muller, 1783) Peters, 1927. (The vinegar eel)

Synonyms.—*Vibrio aceti* Muller, 1783; *Anguillula aceti* (Muller, 1783) Muller, 1786; *Gordius aceti* (Muller, 1783) Oken, 1815; *Rhabditis aceti* (Muller, 1783) Dujardin, 1945

This worm is the common "vinegar eel," which is frequently present in various types of fermenting liquids containing acetic acid. The worm is cylindrical in shape, with a slight anterior and considerable posterior tapering, and possesses a

non-striated transparent cuticula The male measures 1 to 2 mm. in length by 24 to 40 μ in diameter, has two equal spicules 38 μ long, the shafts of which are more or less completely closed tubes, and in addition, a keel-shaped gubernaculum It also has two pairs of preanal, one pair of adanal and one pair of postanal papillæ (all ventral), as well as one pair of postanal dorsal papillæ, but it lacks a bursa or alæ. The female measures 2 4 mm. in length by 40 to 72 μ in diameter, and is viviparous, giving birth to rhabditiform larvæ measuring 222 μ long and 12 μ in diameter. Development is direct.

Human cases harboring this worm have, with one exception, all been women, in

male, in whose sample of alkaline urine specimens of the worm were growing abundantly. The worms were at first confused with *Strongyloides stercoralis*, but later definitely identified as the vinegar "eel" In the sample of urine examined it was not possible to exclude the possibility of external contamination. No significant clinical symptoms have been reported.

Family STRONGYLOIDIDÆ Chitwood and McIntosh, 1934

This family was erected for those species with a typical rhabditoid free-living development, but also having a parasitic phase in which the females are "filariform" in type, adapted to tissue invasion The single species parasitizing man belongs to the

GENUS STRONGYLOIDES GRASSI, 1879

(genus from στρογγύλος, round, and εἶδος, similar)

Strongyloides stercoralis (Bavay, 1876) Stiles and Hassall, 1902.

(The human threadworm, causing strongyloidiasis or strongyloidosis.)

Synonyms.—*Anguillula stercoralis et A intestinalis* Bavay, 1877, *Strongyloides intestinalis* (Bavay, 1877) Grassi, 1879, *Leptodera intestinalis* Cobbold, 1879; *Pseudorhabditis intestinalis* Perroncito, 1881; *Rhabdonema strongyloides* Leuckart, 1883, *Rhabdonema intestinale* Blanchard, 1886

Historical Data.—In 1876 Normand discovered in the feces of French soldiers, who had returned from Cochin China suffering from diarrhea, a large number of minute nematodes, which Bavay described the next year as *Anguillula stercoralis* Five of the patients died as a consequence of the diarrhea and, at *postmortem*, Normand recovered numerous other nematodes from their small bowel, biliary and

the same species, which was heterogenetic in its development. Askanazy (1900) found that the parasitic females live in the wall rather than in the lumen of the intestine, and provided an excellent description of the tissue damage produced by

parasitic females had been found In 1932 Kreis discovered and described the parasitic males, which observation Faust (1933) confirmed Fulleborn (1914) demonstrated that adolescent female worms at times entered, matured in, and produced progeny in the respiratory epithelium This was confirmed by Faust

(1933, 1935), who also traced the stage-by-stage development of both female and

method of internal reinfection (*hyperinfection*), in which infective-stage larvæ *developed in the bowel and penetrated the intestinal mucosa*, so that they reached the lungs through the portal or accessory portal venous circulation, and by this internal route were in a position to proceed with their subsequent migration to the bowel. Sandground (1926, 1928) contributed important biological data on the development of *Strongyloides*, while Beach (1936) was able to cultivate several successive free-living generations of monkey *Strongyloides* and Graham (1936) succeeded in infecting rats after inoculating them each with a single infective-stage larva.

America but is relatively uncommon in China and French Indo-China (Galliard, 1939). Generally, strongyloidiasis is coextensive with human hookworm infection, but there are differences in distribution which have not been satisfactorily explained In northeastern Brazil MacCreary and Bricker (1947) have discovered 12 8 per cent incidence in stools of 133 persons. Infection rates as high as 20 per cent have been reported from Panamá (Darling, 1911; Faust, 1936), while the incidence among 165 patients in the Santa Casa da Misericordia, Rio de Janeiro is recorded as 24.8 per cent (Lopes Pontes, 1946). López-Chávez (1946) reports 2 per cent infection in Cuba, and Rodríguez (1944), 1 94 per cent in Ecuador. In the United States there are records of autochthonous cases from Louisiana, eastern Tennessee, Cincinnati (Ohio), Kansas City (Missouri), western Pennsylvania, New York City and Rochester, N Y Yet Palmer (1944), in reporting a third case from Rochester, N Y, comments on the paucity of information on the incidence and distribution of strongyloidiasis in the country. In 1933 Cadman found this infection in a native of Canada who had always resided there. Stoll's estimate (1947) of world infection is 34 9 millions distributed as follows. 21.0 millions in Asia; 0.9, U. S. S. R.; 0 6, Europe, 3 3, Africa; 8 6, tropical America; 0 4, North America; and 0.1, Pacific islands. Very few basic surveys have been made in endemic areas

Strongyloides fulleborni von Linstow, 1905, a relatively common intestinal parasite of the chimpanzee and African l
duce experimental infection in n
Faust and Kagy, 1933, Tomita,
and Sanders (1948) have reported human infection ... acquired presumably as a result of accidental contamination from the Philippine macaque, *Macaca irus* on Leyte, P I Eggs rather than rhabditoid larvæ were passed in this patient's stools It may be pointed out, however, that in two infections resulting from penetration of filariform larvæ of *Strongyloides* cultured from chimpanzee's feces (Faust and Kagy, 1933; Brannon and Faust, 1949) only rhabditoid larvæ appeared in the fresh semi-formed human stools, although eggs were evacuated in the feces of the chimpanzee hosts.

The Parasitic Generation.—The view first proposed by Leuckart (1882), that the parasitic phase of *Strongyloides stercoralis* consisted of a protandrous hermaphrodite was later abandoned for Rovelli's theory (1888) that the female of the parasitic generation was parthenogenetic. Studies by Sandground (1926) inclined to the belief that the parasitic females are syngonic, while the discovery of parasitic males (Kreis, 1932) and of successive stages of immature males (Faust, 1933) suggested the likelihood that adolescent females may be fertilized before invading the intestinal

(or respiratory) epithelium. On the other hand, Graham's work (1936) indicates that in *S. ratti* parthenogenesis occurs in the parasitic phase of the life cycle of this species, and it seems probable that it may occur in the

The parasitic female (Fig. 206 *A*) is a colorless, nearly transparent, filiform object, measuring about 2.2 mm. in length and varying from 30 to 75 μ in transverse diameter. Its integument has very delicate striations. The nearly cylindrical esophagus extends through the anterior third or two-fifths of the body. The posterior end of the body is pointed. The anal opening is ventral in position, a short distance in front of the caudal extremity. The vulva opens ventrad at the junction of the middle and posterior thirds of the body. The ovaries, oviducts and uteri number two each, one set being disposed anteriad and one posteriad. The females bore deeply into the mucous membrane of the intestinal villi and not infrequently into the epithelium of Lieberkuhn's glands and stroma between these glands, where they secure nourishment and later oviposit.

The eggs, which are thin-shelled, transparent, ovoidal objects, measuring *50 to 58 μ in length by 30 to 34 μ in transverse diameter, complete their* development and typically hatch within the intestinal epithelium, whereupon the enclosed organisms escape into the intestinal lumen and are passed in the feces as the so-called "rhabditiform" larvæ. Only in case of severe diarrhea or after strong purgation are the eggs of this species recovered from the feces. The larvæ, when first hatched (Fig. 207 *A*), measure 200 to 250 μ in length by 16 μ in breadth, but they may grow to two or three times this size by the time they are evacuated in the feces. Meanwhile, according to Looss, one moult takes place. The larvæ are rhabditoid, with an elongate esophageal bulbus and a pyriform posterior bulbus, but without the median

true rhabditiform).

of the body and the

just in front of the posterior third of the body. The larvæ are extremely active, but may be so sparse that they cannot be detected in unconcentrated fecal preparations. They differ from rhabditoid hookworm larvæ in being *slightly less attenuate posteriorly and in having a much shorter buccal* vestibule.

The development of these larvæ, once they have escaped from the human body, may be either "indirect" or "direct," apparently depending on the physical and nutritive characters in the *milieu* on which they are deposited. Under optimum conditions Beach (1936), working with monkey strains of *Strongyloides*, was able to produce only free-living males and females; when conditions were less favorable, he obtained infective-stage (filariform) larvæ.

"Indirect" and "Direct" Development.—In case of "indirect" (*i. e.*, heterogenetic) development, the rhabditoid larvæ moult and within twenty-four to thirty hours are completely developed into sexually mature males and females (the free-living unisexual adults). These worms (Fig. 206, *B*, *C*) are essentially different in size, shape and internal organization from the parasitic female.

The male measures about 0.7 mm. in length by 40 to 50 μ in diameter and the female 1 mm. in length by 50 to 75 μ in diameter. Both sexes have an esophagus similar to that of the rhabditoid larva. The male is devoid of caudal alæ but has two spicules with an accessory gubernaculum (Fig. 206 *E*). The females have a pair of divergent uteri and require fertilization in order to produce viable eggs (Beach, 1936). The thin-shelled, transparent eggs measure 70 by 40 μ. In old females of the free-living generation

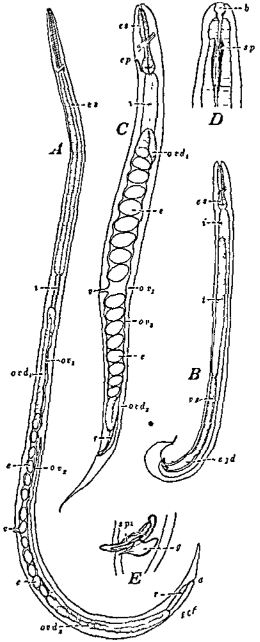

Fig. 206.—*Strongyloides stercoralis*. *A*, parasitic female, × 75. *B*, free-living male, × 160, ... × 500. *E*, copulatory spicules

C, f

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the eggs may hatch *in utero*. The rhabditoid larva which escapes from the egg-shell is distinguished only with difficulty from that developed by the parasitic female After three or four days these rhabditoid larvæ moult and usually metamorphose into elongate filariform larvæ, which are the infective stage for the host.

In the case of "direct" (*i. e.*, hologenetic) development the rhabditoid larvæ evacuated in the feces moult and become transformed directly into filariform larvæ, without the intercalation of the free-living generation The in-

the same stage of hookworm larvæ, but are ordinarily somewhat smaller and always have a minute notch at the caudal tip, a character lacking in the hookworm larvæ.

The filariform larvæ, developed either directly as the progeny of the parasitic generation, or as the progeny of the free-living generation, usually enter the mammalian body *via* the skin, penetrate through the dermal tissues into the venous circulation, thence through the right side of the heart into the lungs, breaking out from the pulmonary capillaries into the alveoli and, after ascending the respiratory tree to the epiglottis are swallowed and descend to the intestinal tract. On arrival in the small bowel, usually at the levels of the duodenum and jejunum, the females burrow into the mucosa and grow into adult worms.

The adolescent male worms, on arrival in the duodenum or jejunum, are apparently incapable of burrowing into the mucosa, but develop into adults in the lumen of the intestine. They may become superficially attached to the mucosa but are easily dislodged and in a few months have been evacuated. Thus they play no rôle in the pathology of the intestinal infection

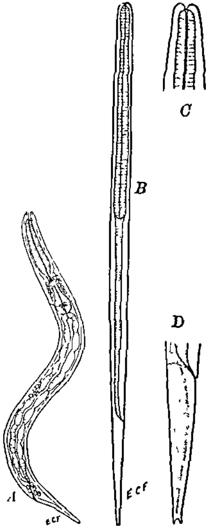


FIG 207 —*Strongyloides stercoralis* *A*, rhabditoid larva, × 310, *B*, filariform larva, × 120, *C*, *D*, anterior and posterior ends of filariform larva, × 640 (*A*, from Faust, after Looss, *B*, *C*, *D*, original) Compare *A* with Fig 221

Mature filariform larvæ of the genus *Strongyloides*, like those of *Ancylostoma*, may occasionally be ingested as a contamination, and, on being swallowed, may burrow into the intestinal mucosa and grow directly into mature individuals. Seventeen days or more are required from the time

of invasion until the worms are maturė and rhabditoid larvæ appear in the feces, occasionally in the sputum, or rarely in the urine.

Autoinfection.—In certain patients, either those heavily parasitized and acutely ill with the disease or chronic carrier cases, rhabditoid progeny of the parasitic females, *en transit* down the bowel, become transformed into filariform larvæ (Fülleborn, Nishigori, Faust). These larvæ are capable of penetrating the intestinal mucosa or the perianal skin without need for

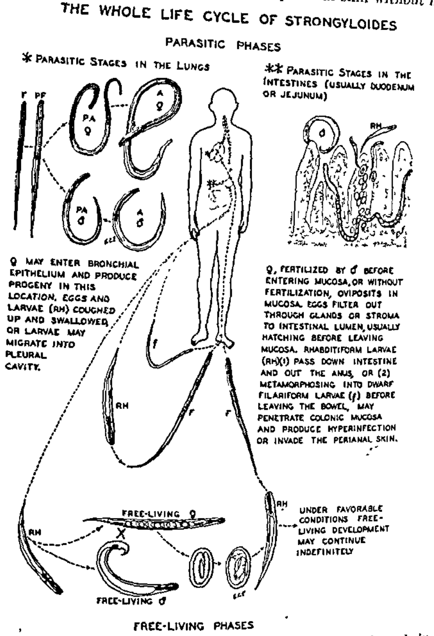


FIG 208 —Diagrammatic representation of the several phases in the life cycle of *Strongyloides* (After Faust, Rev. de Parasitol, Habana)

further development on the ground. By way of the visceral venous blood (from the intestinal mucosa) or the cutaneous venules (from perianal or perineal skin) they reach the lungs, then break out into the respiratory passages and proceed to the intestinal tract just as in persons exposed from

the soil. Fulleborn (1926) stressed the importance of thoroughly cleansing the anal region, particularly after defecation, in order to reduce anal and perianal invasion, while Nishigori (1928), Faust (1933–1936), Nolasco (1936) and Heinert (1947) have provided experimental and *postmortem* evidence in support of internal autoinfection (*hyperinfection*), as a result of larvæ migrating to the lungs *via* the intestinal lymphatics or venous system. Autoinfection logically explains persistent strongyloidiasis in patients who have long since moved from endemic foci.

Occasionally, when the patient's resistance is very low, there may be massive invasion of rhabditoid or filariform larvæ through the intestinal wall, with a fatal culmination (Ophuls, 1929; Torres and Penna de Azevedo, 1938; Faust and De Groat, 1940, Hartz, 1946, Heinert, 1947)

The life cycle of *Strongyloides stercoralis* is epitomized diagrammatically in Fig. 208.

The Hosts of S. Stercoralis and Related Species.—Man is probably the optimum host of *Strongyloides stercoralis*, although the worm which commonly parasitizes the chim[
indistinguishable from the
indistinguishable from this
Japan, India and the Southe
implanted in this host for several months but eventually dies out. Cats and apes have been infected with the worm but it appears to be a very transient parasite in these latter hosts Closely related species occur in the following natural hosts. *Cebus hypoleucus* (*Strongyloides cebus* Darling, 1911), *Anthropopithecus troglodytes* and *Cynocephalus babuin* (*S. fulleborni*

Ransom, 1911), sheep, goats, rabbits, rats, pigs, etc. (*S papillosus* [Wedl, 1856] Ransom, 1911), horses (*S. westeri*, Ihle, 1917), dogs (*S. canis* Brumpt, 1921), macaques (*S simiæ* Lu and Hoeppli, 1923), *Hydrochœrus hydrochœra* (*S. chapini*, Sandground, 1925) and *Mus norvegicus* (*S. ratti* Sandground, 1925). Apparently none of these species is capable of becoming permanently established in the human intestinal tract

Epidemiology.—In the direct mode of development *Strongyloides stercoralis* is characteristically discharged in human feces as a rhabditoid larva and, on contact with moist, shaded soil, metamorphoses into the filariform or infective-stage larva. In general, as Blackie (1946) has found in Northern Rhodesia, strongyloidiasis tends to parallel hookworm infection both with respect to incidence and to geographical distribution; yet there are areas, as in Central and South China where hookworm disease is very important but strongyloidiasis is relatively scant, while strongyloidiasis at times develops to hyperendemic proportions in mental institutions where hookworm infection is relatively unimportant. In the indirect mode of development, following deposition of rhabditoid progeny of the parasitic generation, at least one free-living generation, and potentially an indefinite number, develop on the soil before infective-stage larvæ are developed. Thus, wherever conditions in the soil are favorable for indirect development, as they frequently are in moist, warm climates, there is potentially a much

greater "seeding" of the soil with infective-stage filariform larvæ (*i. e.*, at least one multiplicative stage) than there is in regions where only direct development takes place. Yet this is not the whole explanation; there probably are other, as yet inadequately elucidated factors which may be responsible for direct or indirect trends in the development of the organisms. Possibly these may be associated with the host during the parasitic phase of the life cycle.

The usual source of infection is contaminated soil and the usual portal of entry is the human skin, although invasion of the buccal mucosa is even simpler and more rapid for the invading larvæ. A third mode of infection is autoinfection (*i. e.*, the penetration of the intestinal mucosa [hyperinfection] or the perianal skin by infective-stage larvæ precociously developed in an infected individual without contact with the soil). Autoinfection explains long maintained infections in patients who have resided for many years outside endemic foci.

...tially a disease of warm, moist climates.

[illegible]

period, (2) the *acute stage*, and (3) the *chronic stage*.

1. *The incubation period.*—The infective, filariform larvæ, on entering the skin, produce a dermatitis of the same type as that arising from the invasion of hookworm larvæ, including a painful nettling at the sites of invasion, a local erythematous swelling, and pruritus of the area for several days in case the skin is briskly rubbed. A few days later a mild to severe bron[illegible] ...ree of exposure and [illegible] with an accompanying hacking cough and an elevation in temperature, due to multiple small hemorrhages in the air sacs as the larvæ break out of the pulmonary capillaries, followed by cellular infiltration into the bronchioles, as well as [illegible] ...tabolites of the larvæ [illegible]

2. *The acute stage.*—Upon arrival in the upper [illegible] tine and invasion of the intestinal mucosa, the young females provoke a catarrhal inflammation more or less severe, while the mature worms, in migrating through the villi and gla[illegible] ...ovipositing, and the young larvæ in escaping from the mucosa, [illegible] the glands, and frequently give rise to a [illegible] severity.

The [illegible] and jejunum are the levels of the bowel most commonly [illegible] ...itic females and their and n[illegible] progeny [illegible] wall of the stomach, the appendix and the rectum [illegible] has been found infected in experimental dogs. In one necropsy [illegible] (1946), in Curaçao, Dutch West Indies, found almost no ulceration of the

intestinal wall; the parasitic females were embedded in the stroma of the villi, and their eggs and larvæ in the mucosa of the crypts and the villi. Some larvæ had penetrated through the muscularis mucosæ into the submucosa, muscular coats and subserosa, especially *via* lymphatic vessels; they had provoked a severe, usually granulomatous reaction, with an abundance of enveloping histiocytes.

In heavy infections, involving multiple small patches or extensive areas of the bowel, the worms and their larval progeny honeycomb the mucosa and occasion considerable denudation. This at times results in a persistent, watery diarrhea, with rapid dehydration and emaciation, accompanied by complete exhaustion and death, unless appropriate therapeusis is instituted. More frequently diarrhea alternates with

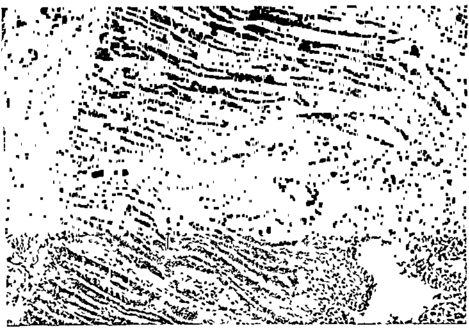


FIG. 209 —Photomicrograph showing the position of the parasitic female *Strongyloides stercoralis*, indicated by arrows, in the duodenal mucosa of an experimentally infected dog × 100 (After Faust, Arch Path)

constipation. The diarrheal state is accentuated by dietary indiscretions, especially by the use of hot condiments. In many individuals harboring a considerable number of parasitic females there is little specific evidence of symptoms. Sooner or later, however, these patients usually develop a nervous syndrome, consisting of "nervous dyspepsia," marked restlessness,

from the bowel wall to transform into infective-stage larvæ before being

evacuated. This exposes the patient to reinfection by the *internal (hyper-infective)* or perianal route. In pati[illegible]

[illegible]

[illegible] de Azevedo, 1938; Faust and De Groat, 1940; Hartz, 1946.)

In addition to strongyloidiasis of the intestinal tract the infection may become established in other organs. The most common of these is the lungs. As mentioned above, adolescent female worms at times invade the bronchial mucosa, mature and discharge their eggs into the tissues. These hatch and the rhabditoid larvæ become transformed *in situ* into filariform larvæ which are voided in sputum. Laptev (1945) reported a case of right-sided bronchopneumonia, with a 22.5 per cent eosinophilia. There was no evidence of intestinal infection but adult worms were recovered from the sputum. Moreover, Whitehall and Miller (1944) reported a male patient with strongyloidiasis of the genito-urinary tract, with a history of lower abdominal discomfort after eating, nocturia, incontinence with respect to urination and diurnal urgency. The feces were negative but motile *Strongyloides* larvæ were recovered from the urine. Cultures produced free-living males and females.

Cerebral lesions in strongyloidiasis probably occur from time to time, due to passage of filariform larvæ through the pulmonary capillaries and their entry into the systemic circulation. Yamaguchi (1925) and Faust (1935) described hemorrhages in the meninges and in the perivascular tissues of the brain, particularly of the cerebellum, in dogs experimentally infected with human strains of *S. stercoralis*. Larvæ were found free in the brain, in the arterioles and capillaries, the ventricles and the choroid plexus. Before sacrifice three of the animals became tetanic, with spasticity of the left extremities and the right side of the face, while another had a syndrome suggesting rabies.

Towards the end of the incubation period and during the early part of the acute stage there is characteristically a leukocytosis of 25,000 or more, with an eosinophilia of 25 to 35 per cent (occasionally as high as 75 per cent or more). Later, as the infection becomes chronic, there is usually a moderate lymphocytosis with slight eosinophilia (6 to 8 per cent) and a neutrophilic polymorphonuclear leukopenia. There is usually an eosinophilic infiltration around the worms in the bowel wall.

Diagnosis.—For intestinal strongyloidiasis this is based on the recovery of the typical rhabditoid larvæ (Fig. 207 *A*) from the feces, or from samples obtained by duodenal drainage (da Silva, 1946). These need not be confused with the progeny of hookworm infection, since in the human bowel the latter develop *in ovo* to the rhabditoid stage only in case of pronounced constipation and rarely hatch in the unevacuated feces. In the average [illegible]

[illegible]

Aids, pp. 592, 594, 599) may be required. Likewise, in patients with watery diarrhea and in advanced chronic cases dwarfed filariform larvæ may at times be recovered from the feces. In pulmonary infections larvæ

or even parasitic females may be recovered from the sputum and rarely the pleural exudate may contain them (Fróes, 1930). In two instances they were found in urine (Fornara, 1923; Whitehall and Miller, 1944). If the feces are allowed to stand for thirty hours or more, the free-living generation may have developed.

Therapeusis.—While many therapeutics have been tried, only gentian violet has been found to be specific for the infection. In order to eradicate the intestinal infection it is necessary for the drug to stain (and thus kill) the female woi 928) first used gentian violet and found the drug helpful. then clinically (Faust 1930, 1936) and found it to be lethal for the parasitic females in case it reached the worms in sufficient concentration. It was also usually well tolerated by the patient. The therapeutic course for *oral administration* consists of 2 one-half grain (0.03 Gm.) Seals-Ins 1½-hour-coated tablets of *gentian violet medicinal*, taken three times daily before meals, for a period of sixteen days (total, 48 grains or 3.2 Gm. For children the daily dose is 0.01 Gm ($\frac{1}{6}$ grain) per year of apparent age. It is necessary to employ the medicinal rather than the biological gentian violet, since the latter is *diluted with dextrin. Furthermore, it is essential to have a* coating which provides a maximum release of the drug at the level of the duodenum, where the greatest concentration of the parasitic worms occurs. One or two courses of treatment are usually curative. Occasionally patients are either refractory to this method of treatment or are unable to take prolonged treatment. For these cases *transduodenal intubation* of 25 cc , 1 per cent solution, of gentian violet medicinal is recommended. The tube is introduced under a fluoroscope, the patient then lies down and the solution is slowly introduced. The tube is left in place for an hour after intubation, then carefully withdrawn. Even if the intubated solution is vomited, and this possibility should be anticipated, the dye in solution has usually penetrated the mucosa of the duodenum and jejunum deeply enough to reach (and kill) the mother worms.

Intravenous therapy.—In case of *Strongyloides* infection in the respiratory tract or elsewhere outside the intestinal tract, the oral administration of gentian violet is not satisfactory. With care a freshly filtered, one-half per cent solution of the drug may be administered intravenously, not in excess of 20 cc. each day every other day for two weeks. The patient must be hospitalized and kept under professional supervision following treatment.

The oral administration of gentian violet medicinal is usually not ients iting , the the gastric mucosa but is usually well tolerated by the intestinal mucosa. When introduced intravenously, a temporarily violet coloration of the skin occurs and there may be some elevation of temperature. There may be a feeling of uneasiness on the part of the patient for an hour after this treatment due to temporary stimulation of the heart, but if he is kept quietly in bed there should be no serious sequelæ. For intravenous use

physicians are cautioned not to utilize a solution more concentrated than one-half per cent or in excess of ...

Prognosis. ... good to fair ... overwhelmi... the prognosi... is grave.

Control.—Since infection is due originally to contact of the skin with soil previously polluted by infected human feces, sanitary disposal of human excreta constitutes the fundamental preventive measure and care not to step barefooted on, or otherwise expose the skin to, infected soil constitutes the second precept. Persons already infected should be given the benefit of specific therapy in order to forestall autoinfection, while the anal region should be kept clean and precautions must be taken to keep the bowel open to reduce the possibility of internal autoinfection.

SUPERF... ...D CHITWOOD, 1937
...1931–1932)
...zky, 1922

The members of this family are free-living saprozoites or parasites on plant tissues. The pharynx in the adult worms is modified into a protrusile spear or onchium. The presence of members of this family in the digestive tract of man is purely accidental.

GENUS TYLENCHUS BASTIAN, 1865
(genus from τυλίζω, to entwine, and ὄγκος, onchium or lancet)

Tylenchus dipsaci (Kuehn, 1858) Gervais and van Beneden, 1859 (the stem or bulb eelworm).

Synonyms.—*Tylenchus putrefaciens* Kuehn, 1879; *Anguillulina putrefaciens* (Kuehn, 1879) Braun, 1895; *Trichina contorta* Botkin, 1883.

This species is a common parasite of the bulb of onions. It has been recorded once by Botkin (1883) in the vomitus of a patient who had previously had a meal of onions.

GENUS HETERODERA SCHMIDT, 1871
(genus from ἕτερος, different, and δέρη, neck)

Heterodera marioni (Cornu, 1879) Goodey, 1932.

Synonyms.—*Anguillula radicicola* Greef, 1872; *Tylenchus radicicola* (Greef, 1872) Oerley, 1880; *Caconema radicicola* (Greef, 1872) Cobb, 1924; *Heterodera radicicola* of authors, *nec. H. radicicola* (Greef, 1872), which is a species of *Turbatrix* (fide Goodey, personal communication, 1941). *"Oxyuris incognita"* Kofoid and White, 1919.

...

thread-like in appearance with an average length of 1.6 mm. and a transverse diameter of 30 μ. The anterior and posterior ends taper to a blunt point. There are no alæ. The cuticula is transversely striated. Anteriorly there are six labia, four of which have minute papillæ. The esophagus is a cylindrical organ about 100 μ long, terminating posteriorly in a spherical cardiac bulbus. The intestine lies in the posterior three-fourths of the body, opening through the rectum into the cloaca at its caudal end.

The mature male worm is typically rhabditoid in shape. There are two testes, which coalesce posteriorly to form a single tubule which is continuous with the unpaired vas deferens. This canal opens into the cloaca just anterior to the rectal opening. There are two slightly curved copulatory spicules of equal length, measuring 34 to 39 μ, guarding the outer opening of the genital canal.

The gravid female is pyriform, lemon-shaped or bottle-shaped, and ranges from 0.6 to 0.75 mm. in length by 0.4 to 0.5 mm. in diameter, being broadest in the posterior third. Both the onchium and esophagus are considerably smaller than in the male. The intestine is tremendously swollen to accommodate the large amount of food consumed. The two ovaries are concealed by the food mass, but the converging uteri can be made out by the eggs which they contain. The vulvar opening is only slightly anterior to the cloacal pore. The eggs which are laid by the gravid female measure 82 to 120 μ in length by 24 to 43 μ in breadth, are elongated ovoidal with rounded ends and are either flat or slightly concave on one side. At the time of oviposition segmentation is just commencing but the embryos soon develop by equal cleavage stages successively into morula, gastrula and motile larvæ (Fig. 211, *1–4*). The larva on escaping from the egg-shell measures from 345 to 370 μ in length. It is readily recognized as a young tylenchid. It may remain and develop in the same roots as its parents, but in case of decay of the host tissues it migrates into the soil, and whenever possible penetrates into a new root, where it begins to consume food ravenously. Upon reaching its full development (*ca* 400 μ in the worm comes to possess differentiating male or female genital organs. It now moults a second *time and transforms into an adult worm.*

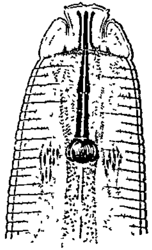


FIG. 210.—Anterior end of *Heterodera marioni*, greatly enlarged, showing onchium. (After Cobb, Journal of Parasitology).

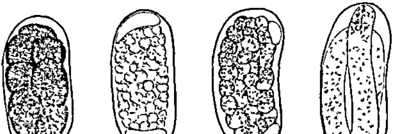


FIG. 211.—Stages in the maturing of the egg of *Heterodera marioni* X ca 400. (After Sandground, Journal of Parasitology.)

The interest of this worm to students of human helminthology lies in the fact that the eggs in parasitized vegetable tissues which are ingested by man are set free in the human digestive tract and are evacuated in the feces, so that fecal examination would seem to indicate the presence of a nematode inhabitant of the human bowel. Keller (1935) states that these eggs may be inaccurately diagnosed as infertile *Ascaris* eggs or hookworm eggs, and thus occasion unnecessary administration of anthelmintics. Sandground (1923) has shown that the eggs designated by Kofoid and White (1919) as "*Oxyuris incognita*" belong to this species of nematode.

CHAPTER XXVI

THE PHASMID NEMATODE PARASITES OF MAN
(Continued)

STRONGYLOIDEA, TRICHOSTRONGYLOIDEA AND METASTRONGYLOIDEA

(Hookworms and Related Forms)

Suborder Strongylina (Railliet and Henry, 1913) Pearse, 1936

(Synonym, Strongylata Railliet and Henry, 1913)

The species of this suborder consist of forms which are covered with a smooth cuticula. They lack valvular lips; at times the buccal capsule is wanting.
worms. T
six paired :
two, equal or unequal. There are ordinarily two ovaries. The eggs are thin-shelled, transparent and are in the early stages of segmentation when oviposited. This suborder has three recognized superfamilies, **Strongyloidea** (Weinland, 1858) Hall, 1916, **Trichostrongyloidea** Cram, 1927, and **Metastrongyloidea** Cram, 1927. Of these superfamilies the type superfamily **Strongyloidea** contains the largest assemblage of species, many of which are of considerable economic significance.

Superfamily Strongyloidea (Weinland, 1858) Hall, 1916

In this group the buccal capsule is well developed. The males have a broad conspicuous bursa. The females are all oviparous and the eggs, on developing, give birth to rhabditoid larvæ. No intermediate host is required. These larvæ may directly infect the host without metamorphosis (*Œsophagostomum*, *Syngamus*) or may require a period of feeding followed by transformation into the filariform type before they enter the host (*Ancylostoma*). In the former case the common mode of invasion is passive, *i. e.*, *via* the mouth; in the latter case, it is usually active, *i. e.*, *via* the skin or oral mucosa. But mature filariform larvæ of the hookworm, upon being ingested, may pass through the stomach uninjured and develop directly into adults in the small bowel. Species of *Œsophagostomum*, upon being ingested, pass through the stomach and small intestine directly into the colon, where they burrow into the wall, and complete their larval development, later emerging into the lumen and becoming attached by their heads to the colonic mucosa. The species reported from man belong to three families, **Strongylidæ** Baird, 1853, **Syngamidæ** Leiper, 1912, and **Ancylostomatidæ** (Looss, 1905).

Family STRONGYLIDÆ Baird, 1853

Species of this family have a conspicuously wide buccal capsule without teeth or cutting plates but with a chitinized corona radiata. The vulva lies in the posterior half of the female's body. The copulatory spicules of the

male are well-developed and equal; a bursa is present. Adults of these species are found attached to the digestive tract of their hosts.

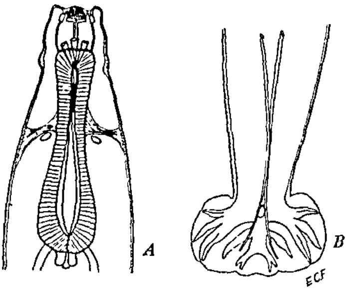
GENUS TERNIDENS RAILLIET AND HENRY, 1909

(genus from *ter*, thrice and *dens*, tooth)

Ternidens deminutus (Railliet and Henry, 1905) Railliet and Henry, 1909.

Synonyms.—*Triodontophorus deminutus* Railliet and Henry, 1905. *Globocephalus macaci* Smith, Fox and White, 1908.

Biological, Geographical and Epidemiological Data.—This species was first described by Railliet and Henry from two specimens, male and female, obtained by Monestier, a surgeon of the French marine, at autopsy of an African Negro in 1865 (habitat, Mayotte, off the coast of Portuguese East Africa.) Sandground (1929, 1931) reports this worm to be common in natives of Southern Rhodesia (50 to 65 per



cent) but rare in Portuguese East Africa. Other cases have been reported by Leiper from natives of Nyasaland and from Portuguese East Africa, and by Noc and Barrois, as well as by Brumpt and other workers, from macaques, the gorilla and other simian hosts.

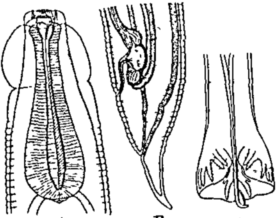
Grossly these worms are apt to
readily distinguished from the latt
oral capsule, which, in *Ternidens*,
bristles. The worms are cylindro... ...its innermost aspect three comp...

double.

The males measure 9.5 mm. in length by 0.56 mm. in diameter. Subcaudally they are slightly attenuated, while the posterior extremity is drawn out into a flange-shaped bursa (Fig. 212*B*), with characteristic rays. The margin of the bursa is

delicately serrated. The spicules are long, stout bristles, measuring approximately 0.9 mm. in lengt
thin posteriorly,
The females m
vulva forms a distinct protuberance a short distance in front of the anal opening.

Clinical Data.—According to Sandground, these worms inhabit the wall of the large bowel, where they may at times produce cystic nodules, but otherwise give rise *to no apparent pathology. They produce no significant anemia* Carbon tetrachloride and tetrachlorethylene are moderately efficient in removing the mature worms from the intestine.



A B C

FIG. 213 —*Œsophagostomum apiostomum* *A*, anterior end of worm; *B*, posterior end of female, *C*, posterior end of male × 50. (*After Railliet and Henry, in Brumpt, Précis de Parasitologie*)

GENUS ŒSOPHAGOSTOMUM MOLIN, 1861

(genus from οἰσοφάγος, esophagus, and στόμα, mouth)

Œsophagostomum apiostomum (*Willach, 1891*) *Railliet and Henry* 1905. (The nodular worm of monkeys.)

Synony
Linstow,
Biologica
parasite of the large intestine of the gorilla, the orangoutang, and the macaque in West Africa It is also present in monkeys in the Philippines and in China. It has been reported from man in Northern Nigeria, where 4 per cent of the prisoners in jails harbor the parasites, and from Lake Omo, East Africa.

The worms are covered with a transversely striated cuticula, which is dilated anteriorly between the excretory pore and the mouth (Fig 213*A*), to form an ovoid

composed of twelve pyramidal setæ directed anteriad. Within the oral cavity there are three minute, recurved teeth, each arising from one of th ... pharyngeal atrium.

The males measure ...
a campanulate bursa ... supporting rays arranged as in the accompanying figure (Fig. 213C). The copulatory spicules are long and somewhat curved posteriorly. The females measure 8.5 to 10.5 mm. in length by 0.295 to 0.325 mm. in breadth. The vulvar opening is immediately preanal in position (Fig. 213B). The eggs closely resemble those of the hookworm; they measure 60 to 63 μ by 27 to 40 μ.

The life cycle of the worms of this species probably parallels that of other species of the genus, which have been elucidated. The larvæ (mature ensheathed semi-rhabditoid stage) are swallowed, pass undigested through the stomach and small intestine, and, on arrival in the cecum, exsheath and invade the wall, where they provoke nodule formation (Fig. 214). The larvæ mature in the cavities of these nodules, whereupon they break out into the intestinal lumen, become attached to the mucosa and develop into adult worms.

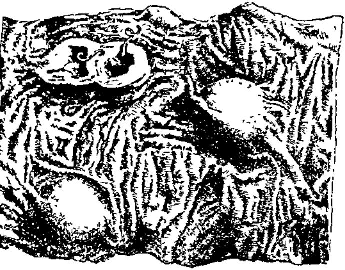


FIG. 214.—Intestinal tumors, with immature *Œsophagostomum apiostomum* in cavities of nodules Natural size. (After Brumpt, Précis de Parasitologie)

consisting of an inner zone of lymphocytes and polymorphonuclear leukocytes

... duce dysenteric symptoms, or may n ...
peritonitis Secondary invasion ... of
Diagnosis.—Practically imposs ... the hookworm.

Therapeusis.—In endemic areas and other regions where this infection is prevalent in reservoir hosts, the patient should be treated with thymol, oil of chenopodium or carbon tetrachloride, which are specific anthelmintics for the adult worms.

Prognosis.—Unstudied.

Control.—Care should be taken not to come in contact with food, water or earth likely to be contaminated with feces of monkeys which commonly harbor the parasite. If Brumpt's hypothesis is correct, danger of infection *via* the skin is as serious as *per os*.

Œsophagostomum stephanostomum var. thomasi Railliet and Henry, 1909.

Biological, Geographical and Epidemiological Data.—This species has been recorded once by Thomas from the large and small intestine of man in Manãos, Brazil. The corona radiata of the buccal capsule has a complement of 38 leaflets. The immature males recovered measure 0 17 to 0 22 mm in transverse diameter. The copulatory spicules are slightly curved at the tip Immature females measure 0 16 to 0.20 mm. in length by 0.9 mm. in breadth and end posteriorly in a short conical appendage. The worm is distinguished in several minor points from *Œsophagostomum stephanostomum* Stossich, 1904, taken from the large intestine of the gorilla.

Pathogenesis, Pathology and Symptomatology.—In the single case on record 187 nodules were found imbedded in the wall of the ileum, cecum and colon. Each contained a single immature male or female worm The formation of fibrous connective tissue in the vicinity of the nodules had been sufficient to reduce considerably the function and capacity of the bowel.

Diagnosis.—Unstudied.

Therapeusis.—Unstidied.

Prognosis.—Unstudied

Control.—Probably the same as for other species of this genus having monkeys and other primates as reservoir hosts.

Family SYNGAMIDÆ Leiper, 1912

The adult worms of this family are typically joined in copula. In the type genus, *Syngamus*, this union is permanent. They possess a large, thick-walled buccal capsule, which is armed at its inner base with 6 to 9 teeth of two distinct sizes. The bursa and supporting rays of the male (Fig. 215 *C*) are characteristically those of the superfamily. In the genus *Syngamus* the spicules are short and thick, and the vulva is situated in the anterior part of the female's body. In *S. nasicola* there are apparently no spicules. The eggs are provided with a cap at each pole in species parasitizing birds but lack these caps in species inhabiting mammals.

Genus Syngamus v. Siebold, 1836

(genus from σύν, together, and γάμος, marriage)

Syngamus laryngeus Railliet, 1899. (The cattle throat-worm, producing syngamiasis or syngamosis.)

Synonyms.—*Syngamus kingi* Leiper, 1913; *Cyathostoma* of St. John, Simmons and Gardner, 1929.

Biological, Geographical and Epidemiological Data.—Members of this family are commonly found in the upper respiratory tract of birds and certain mammals, including cattle, sheep and goats, and felines. The thick-walled buccal capsule is directed anteriad and in the mammalian parasites is armed in its inner base with 8 sub-equal teeth There is a thick muscular inner wall down to the junction with

... and ventro-lateral lips. In the notch between each two lips there is a minute papilla. The male worm is considerably smaller than the female and is permanently joined in copula with her. The copulatory bursa with its supporting rays is generically and specifically characteristic. The copulatory spicules are short and thick. The vulva is situated a short distance anterior to the equatorial plane. The female has an acuminate posterior end. In the species parasitic in birds the eggs have a pair of polar caps, but these are lacking in species parasitizing mammals.

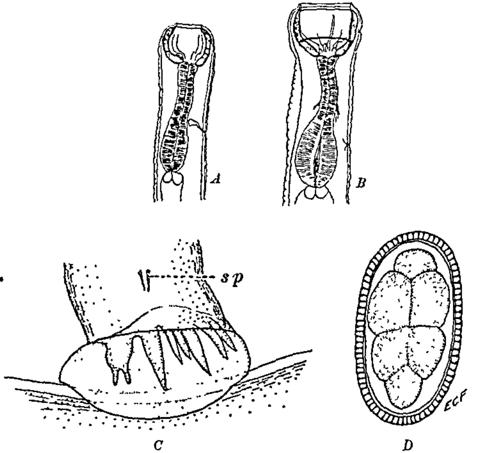


FIG. 215 —Anterior ends of *A*, male worm, *B*, female worm, of *Syngamus* from man, enlarged, (after Leiper, Trans Royal Soc of Med and Hyg), *C*, bursa of male *Syngamus* parasitizing mammalian host, permanently in copula with female, showing lateral view of bursal rays and minute copulatory spicules (*sp*), *D*, egg of *S laryngeus*, × 500, (original).

A pair of syngamid worms in copula was discovered by King in January, 1913, in the sputum of an Irish woman of St. Lucia, West Indies. The pair differed from the ... The

... Leiper failed to record the actual or relative sizes of ... pair, but by inference from other related specimens the female is from two and a half to four times as large as the male. The eggs are not described or figured by Leiper Other cases of human syngamosis have been reported, three times in Brazil (Travassos, 1921; Mello and Mello, 1938; Lent and Penna, 1939), once from the

Philippines (St. John, Simmons and Gardner, 1929), three times from Puerto Rico (Hoffman, 1931, 1932; Faust, one case) and once from Trinidad (Hoffman, 1931, 1932). These are probably all accidental infections by the bovine species, *S. laryngeus*, which inhabits the upper respiratory tract of cattle, water buffaloes and goats in the Orient, in Puerto Rico and in South America, although Buckley (1934) is inclined to refer Leiper's specimens to *S. nasicola*.

Nothing is known of the life history of *Syngamus laryngeus*. The infection in man is undoubtedly accidental and cattle or other herbivores are probably the natural hosts. In *Syngamus trachea* of the domestic fowl the adult worms live in the bronchi

d, are coughed up and

By the eighth or ninth

eak out of the egg-shell

through the polar caps, and are ready for ingestion by the next host. Clapham (1934) has found that earthworms serve as an important intermediate host of the worm, and that the third-stage larvæ are encysted in the somatic musculature of lumbricids Buckley (1934) believes that the same stage of species parasitizing mammals is infective and that an intermediate host is required. Upon being swallowed they become active and migrate through to the lungs where they are found twenty-four hours after ingestion. In the course of a week or shortly afterwards they have paired in the bronchioles, pass out to the larger air passages and attach themselves to the mucous membrane of the bronchi or trachea, where they become sexually mature within three weeks after infection.

Clinical Data.—The worms in the bronchial or tracheal passages produce paroxysms of coughing or sneezing, during which they may be evacuated in the sputum They occasion hemoptysis, at times asthma. Diagnosis in human syngamosis is based on the recovery of the characteristic eggs in sputum Therapeusis has not been studied. The worms are frequently expelled following a paroxysm of coughing. Prognosis is good Prevention is not possible until the source of human infection has been completely elucidated

Other mammalian syngamids include *Syngamus felis*, *S. auris* and *S* *ierei* from

Family ANCYLOSTOMATIDÆ (Looss, 1950) Lane, 1917, emend Nicoll, 1927

The species of this family are popularly known as "hookworms." This designation was originally made (*fide* Stiles) because the bursal rays of the male were erroneously interpreted as hooks (Goeze, 1782). In the subfamily **Ancylostomatinæ** Lane, 1917, *emend.* Nicoll, 1927 the oral cutting organs consist of tooth-like processes, and in the subfamily **Uncinariinæ** Rosenau, 1914 (Syn. Necatorinæ Lane, 1917), of semilunar plates The human representatives of the family belong to the genera *Ancylostoma* and *Necator*.

Genus Ancylostoma Dubini, 1843

(genus from ἀγχύλον, hook, and στόμα, mouth)

Ancylostoma duodenale (Dubini, 1843) Creplin, 1845. (The "Old World hookworm," producing ancylostomiasis duodenalis)

Synonyms.—*Agchylostoma duodenale* Dubini, 1843, *Anchylostomum duodenale* (Dub , 1843) Diesing, 1845; *Anchylostoma duodenale* (Dub , 1843) Chiaje, 1846,

Strongylus quadridentatus v. Siebold, 1851; *Dochmius ankylostomum* Molin, 1860; *Sclerostoma duodenale* (Dub., 1843) Cobbold, 1864; *Strongylus duodenalis* (Dub., 1843) Schneider, 1866; *Dochmius duodenalis* (Dub., 1843) Leuckart, 1867; *Ankylostomum duodenale* (Dubini, 1843) Bugnion, 1880; *Uncinaria duodenalis* (Dub., 1843) Railliet, 1885.

Historical Data.—*Ancylostoma duodenale*, the "Old World hookworm," is, more correctly speaking, the autochthonous human hookworm of the North Temperate Zone of the Eastern Hemisphere. Although undoubtedly an important cause of disease in ancient times, and probably referred to in the Eber's papyrus (1600 B C), the first authentic records of the worm and the disease for which it is responsible were published by Dubini in 1843, from specimens obtained at the autopsy of a Milanese woman in 1838. In 1878 Grassi and Parona demonstrated that the presence of the worm in the bowel could be diagnosed by the recovery of the eggs passed [illegible]

"encysted motile larvæ (of *Ancylostoma*), at a certain period and stage of their development, when introduced into the human intestinal tract, are capable of [illegible]

that these larvæ, after penetrating through the skin, follow an indirect route of migration to the intestine, *via* the venous system to the lungs, thence out into the air passages and over the epiglottis into the intestinal tract.

Geographical Distribution.—(See pp. 425–429.)

Structure of the Adult Worms.—The mature worms (Fig. 216 *A*, *B*) are cylindrical in shape, roseate-white or ivory-gray in color, slightly narrowed anteriorly, and have the anterior end directed somewhat dorsad. The males measur [illegible] females meas [illegible] capsule (Fig. [illegible] the chemical nature of which is probably not chitin, but is otherwise not definitely determined. The cavity is oval in shape, the transverse diameter being the longer. The outer part of the capsule is made up of articulated grooved portions; the inner part, save for the dental armature, is smooth and unarticulated. Ventrally, on the apparent upper side of the mouth, there is a pair of articulated dental plates, each consisting of two large teeth, solidly joined together, of which the outer is somewhat the larger. The members of the inner pair of teeth are each provided with an inconspicuous median dental process. The cuticula is infolded into the mouth cavity but is pierced by the teeth. Dorsally (*i. e.*, on the apparent lower side of the mouth), there is a plate with a deep median cleft, the two free ends projecting slightly over the e [illegible] is the orifice of the dorsal gland. [illegible] of internal teeth. Ventrolateral to [illegible] outer tooth are the openings of the pair of ducts from the cephalic or [illegible] far as the mid-plane of the body. [illegible]

The esophagus is the direct internal continuation of the buccal cavity. It is lined with a [illegible] Its length is about one-sixth that of the entire worm.

non-chitinous substance and has a triradiate lumen. It is somewhat swollen posteriorly and is guarded at its posterior exit by a trilobed cardiac valvular apparatus. Within the wall of the esophagus there are three esophageal glands, one dorsal and two subventral. The intestine proper

FIG 216 Adult *Ancylostoma duodenale*, *A*, male, *B*, female × 20 (Adapted from Looss)

(chyle intestine or mid-intestine) is the portion of the digestive tube which continues through the greater portion of the worm and joins posteriorly the short rectum. It is the only portion of the digestive tract not covered with

stomodeal or proctodeal cuticle and is the region in which digestion and absorption of food occur. The food of the hookworm consists essentially of the mucous membrane of the host's intestine, together with blood cells and serum escaping from the blood supply of the mucosa. Upon becoming attached to host tissue the worm seizes one or more of the villi (Fig. 218), triturating and gradually sucking in the substance, thus eventually consuming all of the villi around the head of the parasite, and, in so doing, opening numerous capillaries and small venules.

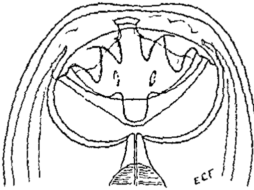


FIG. 217.—Anterior end of *Ancylostoma duodenale*, showing buccal capsule and dental pattern. × 240. (Original.)

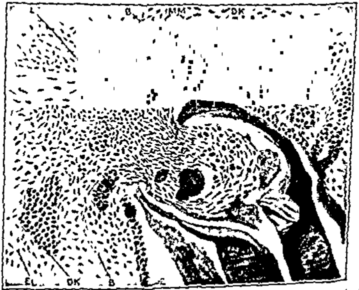


FIG. 218.—Section through human intestine, showing method of attachment of hookworm to the wall. *L*, leukocytic infiltration, *B*, bloodvessel, *MM*, muscularis mucosæ; *DK*, intestinal glands, *E*, epithelium; *EL*, submucosa Enlarged. (After Oudendal, in Transactions of Fifth Biennial Congress of Far Eastern Association of Tropical Medicine, Courtesy of John Bale Sons & Danielsson, Ltd., London.)

The excretory pore is mid-ventral in position, just behind the nerve ring. The e[illegible] ramifica-
tions,[illegible]
cell," and a "suspensory cell." Intimately connected with the [illegible] apparatus are the so-called cervical glands, a pair of elongated, non-glandular cells on the ventral side of the body, extending backwards some distance

behind the esophagus and opening through efferent ducts into the excretory canal system. The excretory canals are embedded in the lateral-line-complex all the way from the buccal capsule to the subcaudal region of the body.

The male worm (Figs. 216*A* and 219) is provided with a campanulate bursa, which is considerably broader than long and gives an expanded appearance to its caudal extremity. The bursa is supported by fleshy rays, the pattern of which is characteristic for the species. The formula for each half of the bursa is as follows: Dorsal ray, single down to its distal third, where it bifurcates, each fork ending in two or three digitations; externo-dorsal ray, arising from the root of the dorsal and extending without forking into the lateral lobe of the bursa; three lateral rays, subequal, well separated and divergent; two ventral rays, close to one another and directed ventrad away from the laterals. The male genital apparatus (Fig. 193, p. 346), if fully extended, would measure more than twice the length of the body. The inner blind end of the testis (*t*) begins a little behind the origin of the cement gland As the tubule proceeds forwards, it becomes wrapped in

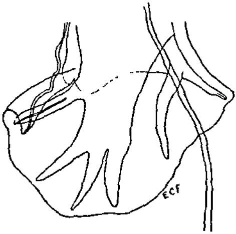


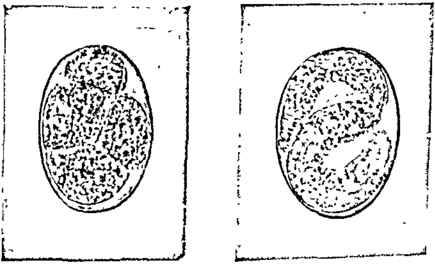
FIG 219 — Posterior end of male *Ancylostoma duodenale*, showing spicules and bursal rays as seen in the left half of the bursa × 80 (Original) Compare with Fig. 226.

transverse coils around the mid-intestine. Upon reaching the posterior aspect of the cervical gland, a longitudinal loop extends forwards for some ... 'eriad as the seminal ... , there to expand into ... ı opens posteriad into ... ıted on either side by the pair of large multicellular cement glands (*cg*), so that the duct and the glands form a supporting trough for the intestine. This structure continues to the subcaudal region of the worm, where the ejaculatory duct, now ...

... gubernaculum (*gub*), which is situated in the dorsal wall of the cloaca and spicular canal.

The female genital organs (Fig. 194, p. 346) consist of two very long ovarian tubules (*ov*), one coiled back and forth in the prevulvar portion of the body and one in the postvulvar part. As they approach the vulva the tubules become appreciably reduced in diameter and proceed for a short distance as oviducts (*od*). Farther outward they become successively differentiated into the seminal receptacles (*rs*), the *uteri* (*ut*) and the ovejectors (*ovj*), the two horns each passing through a vagina (*vg*) and finally joining to form the vulva (*vu*). In *Ancylostoma duodenale* the vulva opens to the outside at the beginning of the posterior third of the body.

Copulating pairs of worms are frequently seen in which the bursa of the male is applied to the vulva of the female, the position being maintained by the insertion of the copulatory bristles into the vulva and by the cementum, elaborated by the cement glands of the male and deposited between the vulva and the bursa.



A B

FIG. 220.—Photomicrograph of eggs of human hookworm. × 666; *A*, 4-cell stage, *B*, egg with motile larva (After Faust, in Brennemann's Practice of Pediatrics, courtesy of W. F. Prior Company.)

Description of the Eggs and Larvæ.—The eggs, on leaving the body of the female worm, are in the early stages of segmentation. (Fig. 220 *A*) They are ovoidal, with bluntly rounded ends and with a transparent hyaline shell-membrane, which is so thin as to appear as a single line under low power of the microscope. While there is considerable variation in their size, they average 60 by 40 μ. When evacuated in the normal stool they are in the two- to eight-cell stages of segmentation. Occasionally unsegmented eggs are found in feces, while, in constipated stools that have remained several days in the bowel, gastrulæ and even unhatched rhabditoid larvæ may be present (Fig. 220 *B*). In moribund females, discharged from the bowel, larvæ may develop *in utero* and may feed on the internal organs of the parent worm.

... il very little development

night-soil is placed on the land for fertilizer ...

egg-containing feces are made on moist, sandy, shaded earth, development proceeds rapidly, so that, under favorable conditions of temperature, hatching takes place in twenty-four to forty-eight hours. The optimum conditions for the hatching of eggs of *A. duodenale* appear to be moist, aerated soil, protected from the direct rays of the sun, with an average temperature of about 25° C. Excess of water, of acidity, or direct sunlight hinders hatching and development.

The larva emerging from the egg is a typical rhabditoid nematode (Fig 221), measuring 0.25 to 0.3 mm. in length, bluntly rounded anteriorly and attenuated posteriorly, and with a maximum diameter of about 17 μ in the anterior third of the body, near the nerve

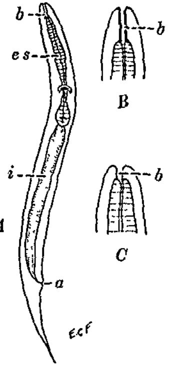


Fig 221.—*A*, rhabditoid larva of the human hookworm, × 300, *B*, anterior end of larva, showing long, narrow, buccal chamber; *C*, Similar view of anterior end of *Strongyloides* rhabditoid larva *a*, anus, *b*, buccal chamber, *es*, esophagus, *i*, mid-gut (Original)

able annulus just in front of the esophagus. The esophagus occupies the anterior third of the digestive tract; it is composed of a cylindrical anterior portion and a pyriform posterior bulbus. The mid-gut consists of a hollow column of alternating dorsal and ventral cells. The rectum is a delicate, slit-like, cuticularized tubule. The anal opening is situated at the beginning of the caudal fifth of the body.

After about three days active feeding on bacteria and possibly organic débris and following growth, the larva moults (first ecdysis), continues to feed and to increase in size up to 0.5 or 0.6 mm., but still retaining its rhabditoid character. At the beginning of about the fifth to eighth day the larva ceases feeding, and a metamorphosis to the filariform type takes place. The mouth becomes closed, the esophagus elongates, and the second ecdysis occurs, although the larva usually remains within the shed cuticula, which becomes shrunken but remains

ions these larvæ are viable in soil up to fifteen weeks. They can be differentiated from the similar stage of *Necator americanus* (Fig. 222 *C*) in that (1) the protrusile esophageal spears are unequal in thickness in *Ancylostoma* (Fig 222 *B*) and equal in *Necator* (Fig. 222 *D*), and (2) the cardiac portion of the esophagus appears to be in direct contact with the anterior portion of the mid-gut in *Ancylostoma*, while in *Necator* an intermediate transverse space appears to be present. After a period of quiescence, or upon the loss of the enveloping moulted cuticula, the larvæ become active again, and, on contact with the human

skin, penetrate the skin layers. Within twenty-four hours or less they reach a bloodvessel, whereupon they are carried through the right chambers of the heart to the lungs, thence after breaking out into the alveoli, are transported up the a
tract to the jejunum
their development.
the jejunum a third ecdysis occurs, and a provisional buccal capsule is

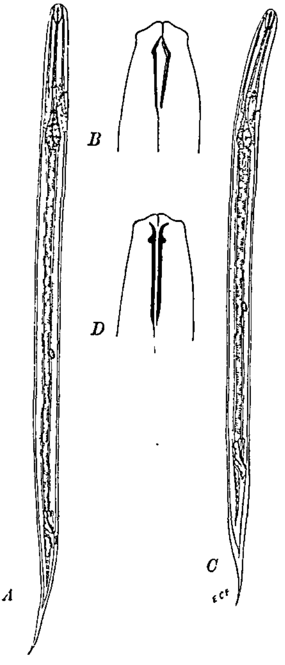


FIG. 222 —Filariform larvæ of hu
(Original adaptation from Looss) B,
spears. (After Heydon, Medical Jo
(Original adaptation from Looss.) D,
buccal spears. (After Heydon, Medical Journal of Australia)

formed, so that the adolescent worms are able to attach themselves to the villi, grow in size, and develop the definitive mouth capsule within the old one. Then the provisional capsule and the fourth cuticle are shed (final ecdysis), and the worms develop into adults.

As Lane (1932) has remarked, "the circulatory escalator, whether blood or lymph, takes (the larva) to the lung capillaries, the bronchial escalator to the larynx, and the peristaltic escalator to its permanent habitat." Looss found that the majority of hookworm larvæ reach the gastro-intestinal tract within twenty-four hours after skin exposure, while more recently Miyagawa and Okada (1930) have concluded that the migration through the lungs is biologically indispensable for development to the adult stage On the other hand, there is some apparently convincing experimental evidence, supporting the view that mature infective-stage larvæ, when introduced directly into the intestine, may for a short time burrow into the glands, after which the majority will become attached to the villi and develop into adult worms without a lung migration.

About five weeks is required from the entry of the filariform larvæ into the skin until egg-laying begins. Mature females of *Ancylostoma duodenale* lay about two to two and a half times as many eggs per day as do the females of *Necator americanus.*

Factors Involved in the Growth of Eggs and Larvæ.—In the undiluted feces
few or no larvæ are
there (pH 4 8 to 5)
however, rains and
deposits. Water not only serves as a vector, but, in diluting or moistening of feces, serves to initiate hatching and growth of the larvæ. However, rapidly moving water is not conducive to development, and heavy rainfall, such as occurs in the Tropics, is a natural sterilizing agent for infected areas. Water covering soils containing large numbers of hookworm larvæ tends to cause rapid death of the larvæ on account of the growth of bacteria, fungi and protozoa which are larvicidal. Alternating drying and moistening of the medium also tend to kill the larvæ

Temperature is an important conditioning factor of growth. While 27° C. seems to be favorable to hatching and development, at this temperature most of the larvæ succumb in nine weeks, although as many as 5 to 10 per cent may survive some weeks longer; at 35° C. the majority die in four weeks, at 15° C growth is slower and the length of life longer. At 0° C. growth is inhibited and death occurs fairly rapidly. Within certain limits the viability of hookworm larvæ in a favorable environment varies inversely as the rate of metabolism. Direct sunlight of the Tropics is distinctly unfavorable for hookworm larvæ in the soil. Dense shade constitutes the optimum for their development and continued existence. Even in light shade the period of viability is reduced.

Dilution of the feces with soil is highly favorable to hatching and development Larvæ have been found to migrate to the surface after having been buried in sandy loam to a depth of 36 inches. Mixtures of clay reduce the range of migration directly with the proportion of this ingredient in the soil. Normally in fecal deposits on the surface of the soil, the greatest number of hookworm larvæ remains in the upper ½ inch of the soil and the number

decreases rapidly with the increasing depth of the soil. They do not migrate out of the soil onto vegetation in the immediate vicinity.

It was formerly believed that the second ecdysis occurred only at the time of human infection. But, in the Tropics, a large share of the larvæ becomes unsheathed in the soil and lives for the normal length of time. It was also formerly believed that larvæ might live in the soil for long periods of time, possibly years, and still remain active (*i. e.*, viable). Under tropical conditions seven or eight weeks appear to be the maximum period of existence. In temperate zones this period is increased as the metabolism of the larva is slowed down. In regions where ancylostomiasis is most prevalent, the disease is probably propagated through constant reinfection of the soil, rapid development of the larvæ, and consequent reëxposure of human beings frequenting such infected spots.

The length of life of the adult worms of this species has been estimated at nine to ten years but recent investigations suggest that this estimate is probably too high. The work of Chandler (1926, 1929, 1935) indicates that, in the absence of reinfection, the egg-count in hookworm patients drops about 50 per cent in the first three months, 60 per cent in six months, 70 per cent in one year, 80 per cent in two years, and 92 per cent in five years. After the ninth year a small number of eggs may still be recovered. Maximum egg production is reached about the sixth month following exposure to infection, after which time egg production in patients on a constant diet fluctuates very little. Thus egg-count constitutes a relatively reliable criterion of the number of worms. However, differences in egg-laying exist in lightly and in heavily infected population groups. Moreover, continuous reinfection constitutes an integral part of the hookworm problem. Retired Hungarian miners have been found to retain their infection in hookworm-free environments for six to eight years after retirement (Lörincz, 1935).

Man is probably the only normal definitive host of this species, although Baylis and Daubney (1923) record a single female worm from a tiger (Calcutta). Likewise, hookworms identified as *A. duodenale* have been reported from the following mammals: pig (O'Connor, 1921; Legg and Rheuben, 1921); lion in captivity (Schwartz, 1927); *Viverra zibetha ashtoni* (Baylis and Daubney, 1922); *Viverricula indica pallida* (Adler, 1922); ca (experimental only); *Megalotis zerda* (McClure, 1932); dog (Miyagawa *fide* Hall, 1923; Thapar, 1929); *Pan* sp., *Hylobates lar* and experimentally *Silenus silenus* (Stiles, Hassall and Nolan, 1929); gorilla (Looss, 1911) experimentally *Silenus sinicus* (Strong, 1930).

Maplestone (1933) obtained a mild "creeping eruption" in three of six tea-garden coolies in India, inoculated percutaneously with infective-stage larvæ of *A. duodenale*.

For a consideration of hookworm disease, its distribution, epidemiology, clinical and preventive aspects, *vide* pp. 430–443.

Ancylostoma caninum (Ercolani, 1859) Hall, 1913. (The dog hookworm, producing ancylostomiasis canina.)

Synonyms.—*Sclerostomum caninum* Ercolani, 1859; *Strongylus caninus* Ercolani, 1859, *Uncinaria canina* (Erc., 1859) Railliet, 1900

This is the common hookworm of the dog and cat. It is practically cosmopolitan in distribution, but is more properly autochthonous in the Holarctic region, being

replaced, at least in part, in the more tropical areas by *A. braziliense*. It is questionable whether it occurs naturally as a parasite of the human host, although it has been reported once from a Filipino (Manalang, 1925). The male worm averages 10 mm in length by 0 4 mm. in breadth and the female, 14 mm. in length by 0 6 mm. in breadth.
any descri
three teetl
The bursa is large and flaring and is supported by typically long and slender rays

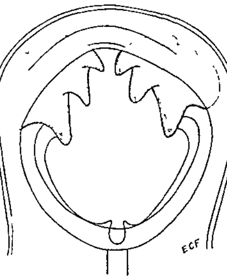


FIG 223 —Anterior end of *Ancylostoma caninum*, showing buccal capsule and dental pattern × 240 (Original)

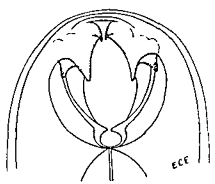


FIG 224 Anterior end of *Ancylostoma braziliense*, showing buccal capsule and dental pattern × 240 (Original)

The copulatory bristles are stout and relatively short The eggs are similar in type to those of *A duodenale*, but are slightly larger, measuring 63 8 by 40 4 μ The life cycle is similar to that of *A duodenale*, but *A caninum* is adapted to a somewhat cooler free-living *milieu* than *A duodenale*. Prenatal infection in dogs has been demonstrated experimentally by Foster (1932) The canine and feline strains of this worm are physiologically distinct (Foster and Daengsvang, 1932)

The infective, filariform larvae of *A. caninum* are probably capable of producing a mild transient dermatitis when brought in contact with the human skin. Moreover,

"creeping eruption" has been described for man a the result of cutaneous inoculation with infective larvæ of this, as well as the European dog hookworm (*Uncinaria stephanocephala*) (Fülleborn, 1927; Heydon, 1929; White and Dove, 1929; Hunter and Worth, 1945).

a wealth of valuable information.

Ancylostoma braziliense Gomez de Faria, 1910. (The hookworm producing "creeping eruption.")

Synonyms.—*Ancylostoma ceylanicum* Looss, 1911; (larva) *Agamonematodum migrans* Kirby-Smith, Dove and White, 1926.

This species of *Ancylostoma* was first found by Gomez de Faria in dogs and cats in Southern Brazil in 1910 and was described by Looss the following year from a human infection in Ceylon. Since that time its presence has been recorded in a number of instances from the intestine of man, of the dog and of the cat in the Oriental region

floridanus) in the environs of New Orleans, Louisiana, and from the leopard in Sierra Leone. In human cases it is usually a minor infection along with *Necator americanus*, in dogs and cats it is frequently found in a predominantly *Ancylostoma caninum* infection In the Southern United States human intestinal infection with this hookworm is unknown except for one report from Texas, but in the Gulf Coast States, especially Florida and eastern Texas, the cutaneous infection or "creeping eruption," as a result of exposure to canine and feline strains of the parasite, is relatively common.

According to Stoll (1947) there are relatively few authentic records of the natural occurrence of adult *A. braziliense* from man, actually less than 200 reported instances. These include cases from Brazil and Texas in the Western Hemisphere, and Bengal, Burma, Siam, Malaya, Sumatra, Java, Philippines, Formosa (?), Fiji and certain islands north of Australia in the Eastern Hemisphere.

The male worm measures 7.75 to 8.5 mm. female, 9 to 10.5 mm. by 0.375 mm. Th that of *A duodenale* in having a somewhat each carry a small, curved inner tooth and a large outer one. male also differs in being short, stubby rays. The The investigations of Kir mature filariform larvæ o by the skin route of invasion; and that larvæ entering the human body via the skin are responsible for h uthern United States. In an attempt to cul ziliense under aseptic conditions, Lawrence were as satisfactory as those in which living bacteria were present. (For clinical aspects of this infection see section on "Pathology and Symptomatology of Hookworm Disease," pp. 435–437.)

Ancylostoma malayanum (Alessandrini, 1905) Lane, 1916.

Synonym.— *Uncinaria malayana* Alessandrini, 1905.

This species of hookworm was first described by Alessandrini (1905) from the Malay bear (*Helarctos malayanus*). In 1916 Lane reported the same worm from the Himalayan bear (*Ursus torquatus*). Yorke and Maplestone (1926) record this worm from man.

The males measure 12 to
mm long by 0 6 mm broad.
most slender of the described

stout. The terminal parts of the dorsal ray are noticeably sinuous. The copulatory spicules are very long (3 mm.) and delicate. The eggs are indistinguishable from those of *A. duodenale*

Genus Necator Stiles, 1903

(genus from *neco*, to kill)

Necator americanus (Stiles, 1902) Stiles, 1903. (The "American hookworm," literally the "American murderer," producing tropical hookworm infection.)

Important Synonyms.— *Uncinaria americana* Stiles, 1902; *Ankylostomum americanum* (Stiles, 1902) v Linstow, 1903, *Ancylostoma americanum* (Stiles, 1902) Siccardi, 1905, *Necator africanus* Harris, 1910, *Necator argentinus* Parodi, 1920.

Historical Data.—This species of hookworm, commonly designated as the "American hookworm" or the "New World hookworm" was described as a new species by Stiles in 1902 from material sent him for examination by Allan J Smith from Galveston, Texas

Hookworm disease, referred to as mal d'estomac, mal de cœur, cachexia, geophagia, etc , was stated by Pére Labat to be present in Guadeloupe as early as 1742 and by Edwards in the British West Indies towards the end of the eighteenth century (1793) In 1845 Little reported the disease in Florida and in 1850 Duncan found it in Louisiana Lutz (1885, 1888) stated that it had a widespread distribu-

"variety." Lutz (1888) also described his specimens from Brazil as different from the "Old World hookworm." Blickhahn (1893) in St. Louis, Herff (1894) in Texas, Moehlau (1897) in Buffalo and Tebault (1899) in New Orleans were apparently the earliest workers to recover human hookworms in the United States. In 1900 Ashford reported twenty cases of tropical anemia in Puerto Rico, nineteen of which he definitely attributed to hookworms (*Ancylostoma duodenale*)

Stiles (1902) first referred his new species to the genus *Uncinaria* but the next year created for it a separate genus, *Necator*. Investigation soon showed that this species was the prevalent form in the Southern United States, the islands of the Caribbean, Central and South America, and that it has a wide distribution and in many localities was a serious menace to life and health Later it was found that it was also the common autochthonous species in the Eastern Hemisphere south of 20 degrees north latitude.

Structure and Life Cycle.— *Necator americanus* belongs to the hookworm subfamily **Uncinariinæ**, distinguished by the presence of semilunar plates and lacking the dental processes characteristic of the buccal capsule of the **Ancylostomatinæ**. The genus *Necator* is further characterized by having in the depth of the buccal cavity two triangular subventral lancets and two subdorsal ones.

Necator americanus is grayish-yellow in color, with an occasional reddish cast The body is cylindrical, and somewhat attenuate anteriorly The

male measures 7 to 9 mm. in length by 0.3 mm. ...
9 to 11 ...
is stron...
small. ... ventral aspect there are two semilunar cutting plates (*vpl*) while on the dorsal side there is a pair of slightly developed ones (*dpl*). A conical dorsal median tooth (*dt*) projects prominently into the buccal cavity. The single pair of lancets (*ll*) in the depth of the cavity are of the type described for the genus. This type of biting apparatus is structurally inferior to that of the members of the genus *Ancylostoma*.

The caudal bursa of the male (Fig. 22... long and wide. The rays for each half of ... pair, bipartite at their tip; a slender, unbranched externo-dorsal ray; a large, fleshy, trifurcated lateral, with the externo-lateral distinctly separated from the medio-lateral and postero-lateral, which are separated only at their distal end, and a cleft ventral pair arising from the inner aspect of the

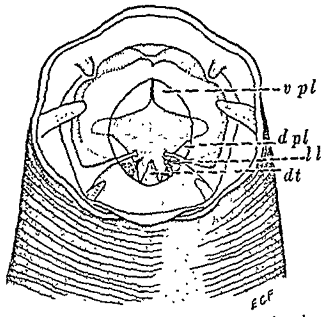


FIG. 225 – Anterior end of *Necator americanus*, looking into the buccal cavity. *dpl*, dorsal cutting plate, *dt*, dorsal tooth, *ll*, lateral lancet, *vpl*, ventral cutting plate. × 400 (Original adaptation from various authors.)

lateral. There is also an inconspicuous accessory prebursal ray anterior to the ventral rays. The two copulatory spicules are long and slender. Their distal ends are fused and are tipped with a delicate barb.

Tl...
lo...

... on the
from the small bowel of the chim...
gorilla (*Gorilla gorilla*) in West ...
Guinea, the pangolin (*Manis jav*...
rhinoceros, and occasionally the do...
to that of *Ancylostoma*, although ...
free-living environment than is *A. duodenale*.

Maplestone (1933) produced typical "creeping eruption" in six out of six tea-garden coolies in India experimentally inoculated percutaneously with infective-stage larvæ of this species. In 1922 Ackert and Payne created the species *Necator suillus* for the hookworm which they recovered from pigs in Trinidad. The validity of this species has been attacked by various workers, including Lane (1932). On the other hand, Buckley (1935) has furnished evidence supporting its specificity, based on morphological, biological and experimental grounds. Physiologically the necators of man and pigs do not provide satisfactory reciprocal infections. It is possible that these two groups of organisms are present-day variants from a single, more primitive, prototype

For a consideration of hookworm disease, its distribution, epidemiology, clinical and preventive aspects, *vide* pp. 425–443.

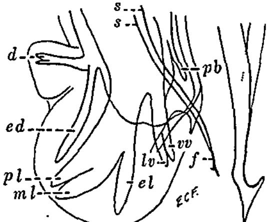


FIG. 226 —Posterior end, lateral view of male *Necator americanus*, showing bursal rays and copulatory spicules, × 80 At the right, greatly enlarged, lateral view of fused termination of the two spicules, ending in a barb *d*, dorsal ray, *ed*, externo-dorsal ray, *el*, externo-lateral ray, *f*, fused terminus of spicules, *lv*, latero-ventral ray, *ml*, medio-lateral ray, *pb*, prebursal ray, *pl*, postero-lateral ray, *vv*, ventro-ventral ray × 50 (Original adaptation)

Nosogeography and Ethnological Distribution of Hookworm Disease.—In spite of the earlier epidemiological studies of Zinn and Jacoby (1898) and of Blanchard (1890, 1900), the problem of the geographical distribution of human hookworms is a relatively new field of investigation. It involves two important critical factors: (1) the areas of land in which climatic conditions are favorable for the growth of the free-living phase of the life cycle of the hookworm in the soil; and (2) the actual incidence of infection of the several species (for practical purposes the two species, *Ancylostoma duodenale* and *Necator americanus*), in indigenous (autochthonous) populations practically or entirely free from foreign contact. The former condition of the environment is usually described as being delimited by those isothermic belts where freezing temperatures do not occur for any considerable part of the year In the United States this line is usually considered the northern boundary of North Carolina and its extension farther west.

In general, the infective zone for hookworm endemicity is limited by 35 degrees north latitude and 30 degrees south latitude, although there are

or have been exceptions to this temperature limit, as for example, warm mines in colder climates (Wales, Central and Northern Europe, California, Illinois, China), and other regions where the sanitary conditions within the homes, such as dirt floors and defecation within the houses, tend to perpetuate the life cycle during winter months. There are, however, large stretches of desert within the thermally potential areas where desiccation prevents the development of the extra-human phases of the life cycle. There are also areas outside of these zones where a minimum infection is harbored, although it is not clinically important.

The original distribution of *Ancylostoma duodenale* and *Necator americanus* is known to have varied considerably from that of its present location.
[illegible] ie migrations of peoples. Due
[illegible] ex of certain peoples has been
entirely modified. Present day information leads us to believe that the original distribution of the hookworms was entirely in the Eastern Hemisphere, and that *Ancylostoma duodenale* occurred north of 20 degrees north latitude and *Necator americanus* south of 20 degrees north latitude. Thus, the ancylostome species existed in Europe and parts of Africa bordering on the Mediterranean; in Northern India, Central and North China and Japan. *Necator* was found in Tropical and South Africa, Southern India, Malaya, Java, Sumatra, Borneo, Celebes, New Guinea, Fiji and other islands of the Polynesian and Micronesian group, Siam, French Indo-China and to a certain extent in southern China.

The migration of peoples accounts for the following present distribution (Fig. 227).

1. *The Americas.*—(*a*) The Southern United States. *Necator americanus* was introduced by the Kaffir and Mosambique slaves from Africa. *Ancylostoma braziliense* is a common intestinal infection of dogs and cats in the Gulf Coast area and Southeastern Atlantic seaboard, but in the human population is confined to a cutaneous infection. (*b*) Central and South America, as well as the West Indies and Mexico; as far south as Argentina. *Necator* has been introduced by the same source as (*a*) and also by Tamils, Bengalis and Javanese. In one province of Brazil where there has been heavy colonization by Spaniards, Italians and Portuguese, the ancylostome-index rises to 11.2 per cent. In another province the relatively high ancylostome-count is due to Japanese colonists. *Ancylostoma braziliense* is present as an incidental intestinal infection of man in this area. (*c*) Little is known about the hookworm infections of the aboriginal Amerinds, either in North America or in the Andean areas, but the investigations of Soper (1926) among the native Paraguayans indicate a very high ancylostome-index.

2. *Europe.*—The only species found in Europe, except in returned colonists from the Southern United States or Brazil is *Ancylostoma duodenale* [illegible] ly, Sicily,
[illegible] the Loire
[illegible] rleroi, and
[illegible]
in Germany, Poland and Silesia. It was the cause of the great epidemic during the construction of the St. Gothard tunnel. *Ancylostoma braziliense* is not known to be present in Europe.

3. *North Africa.*—There is an exclusively *Ancylostoma duodenale* infection in North Coastal Africa.

4. *Tropical and South Africa.*—As far as is known there is an exclusively *Necator americanus* infection in this region, except for an incidental infection with *A. braziliense* and with *A. duodenale* in Portuguese West Africa (de Azevedo, 1938)

5. *The Malay Peninsula* —From native kampongs or villages which are usually separate from the Tamil and Chinese villages, the parasite has been

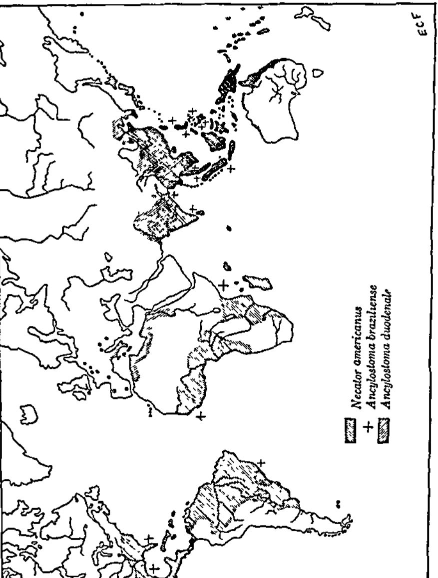


Fig 227 —Map showing the distribution of the important species of human hookworms (Original)

found to be almost entirely *Necator* (only 0.25 per cent ancylostome-index). *A. braziliense* is not uncommon.

6. *Java.*—(*a*) West Java. This is practically the same as that in the Malay Peninsula, *i. e.*, less than 1 per cent ancylostome-index. *A. braziliense* has also been recorded from this part of the island. (*b*) Mid-Java There is a fairly high ancylostome-index (up to 10 per cent) in Central Java, due to contact with the Chinese immigrants.

7. *Sumatra, Celebes and New Guinea.*—*Necator* is usually the predominant species, but the index depends on the contact with Chinese immigrants. *A. braziliense* is present in Sumatra.

8. *Southern India and Ceylon.*—This is predominantly a *Necator* infection, but the ancylostome-index may reach 65 per cent, depending on the number of returned Tamils who have been in contact with Chinese carrying an infection of *Ancylostoma* originally acquired in China. *A. braziliense* is recorded from Ceylon.

9. *Northern India.*—Lane (1916) states that *Necator* is the only form found in the Darjeeling district but Sikhs who have been in contact with *Necator* carriers in the Malay States for ten years or more have an ancylostome-index of 51.2 per cent. Likewise, indentured workers in Fiji, hailing from the Central, United and Northwestern Provinces, after more than five years' residence were found to harbor 27.5 per cent *Ancylostoma*. *A. braziliense* occurs in Northeastern India.

10. *Siam.*—The only form found is said to be *Necator* (Kerr, 1916).

11. *French Indo-China.*—The only form found is *Necator* (Noël Bernard, 1922).

12. *China.*—(*a*) The Cantonese and Hainanese harbor *Necator* up to 90 per cent. The infection with *Necator* is progressively less up the coast to Shanghai, where possibly 50 per cent *Necator* occurs. In North China there are few indigenous infections with *Necator*. Cases in this area with a high *Necator*-index usually give a history of residence in South or Central China. (*b*) The hill tribes of Fukien have been found to harbor a pure *Ancylostoma* infection (Faust and Kellogg, 1929).

13. *Japan.*—The autochthonous infection consists of a pure culture of *Ancylostoma*, but *Necator* has been introduced by returned emigrants and soldiers. *A. braziliense* occurs in Formosa, although *Necator* is the prevalent form.

14. *The Philippines.*—Data show about 12 per cent *A. duodenale* infection (Leach *et al.*, 1923). The incidence of *A. braziliense* is appreciable.

15. *Micronesia.*—There is nearly a pure *Necator* infection in Fiji, where ancylostome carriers have not colonized. *A. braziliense* is occasionally encountered. In natives of Guam Stoll (1946) encountered 76 per cent *A. duodenale*.

16. *Australia.*—The Queensland aborigines are pure *Necator* carriers. In West Australia the aborigines are all *Ancylostoma* carriers.

The data demonstrate that the type of hookworm in a given population at the present day varies on the one hand according to the autochthonous index and on the other according to the I
intermingling of peoples. Chinese have m
the Malay, Dutch East Indies and parts of .

the Japanese and Italian colonization of certain states in Brazil is responsible for the ancylostome infection there The most profound transfer of the hookworm has been that imported into the Americas with the African Negro, and the imposition of this infection upon the American aborigines and European settlers.

Incidence.—Stoll (1947) has estimated the total world incidence of *Ancylostoma duodenale* and *Necator americanus* combined to be 456.8 millions, including 359 millions from Asia, 2.8 from the U.S.S.R., 1 4 from Europe, 49 from Africa, 42 from tropical America and 1.8 from North America.

Epidemiology of Hookworm Disease.—While there is a tremendous literature on hookworm disease, too much stress has been laid on "treatments" and too little has been done in learning about the underlying biological and epidemiological reasons for the existing conditions. Baermann (1917), working on the problem in Indonesia, was the first person to devise a practical method of isolating hookworm larvæ from the soil, and initiated the modern scientific study of the hookworm problem.

There are two prerequisites for undertaking field investigation on this problem: (1) Accurate methods for determining the infective index in the infected population; and (2) similarly reliable procedures for determining the pollution in the soil. The former has become more and more refined until we now have concentration methods (see p 593), which are accurate for all practical purposes. The latter need is met by the Baermann apparatus for the isolation of hookworm larvæ. (For the use of this apparatus see p. 600.)

With these tools at hand and the technic of their use perfected, the first essential step in undertaking a field problem of this nature is the *selection of a typical area* in an infected district, on which and in which the survey is to be made Such a reconnaissance consists of three main parts which, however, are closely bound up with one another: (1) A preliminary survey of a representative group of the population to determine the hookworm index; (2) an investigation of the prevalence and distribution of soil pollution in that area, and (3) a survey to determine the natural and artificial means whereby the cycle of reinfection of the population is perpetuated. The problem has been carefully outlined by Cort (1921) and investigations

the need for an accurate measure of the *worm burden* in an infected population, both before and following treatment. Data on *worm incidence* alone fall far short of the desired end Thus far the only known way of gauging the relative number of worms present in an infected individual is the utilization of the so-called egg-counting technics.

As is indicated in the life cycles of the hookworms *A. duodenale* and *Necator americanus*, warm, moist, shaded, sandy soil, with a considerable amount of decaying vegetation, constitutes the optimum culture bed for hatching, feeding and metamorphosis of the rhabditoid larva into the infective filariform larva On contact with the skin these larvæ initiate infection in man Secondarily, in moist warm climates fæces-soiled clothes

provide an opportunity for eggs in [illegible] larvæ to proceed to the infective sta[illegible] who wash the clothes (Laughlin and Stoll, 1947). *Necator americanus* is [illegible] ntries, [illegible] nates, but today there is much overlapping. Man is the only important host of these two hookworms.

CLINICAL ASPECTS OF HOOKWORM DISEASE

Pathogenesis, Pathology and Symptomatology of Hookworm Disease.—Even before the etiological agent of the disease was known, there was clinical evidence indicating that persons seriously ill with the disease exhibited a variety of digestive disturbances, more or less profound anemia, palpitation of the heart and cachexia. Following the discovery of the hookworm as the causal agent, the elucidation of its usual portal of entry on exposed skin and its migration through the body *via* the lungs to the intestinal tract, the progressive pathology and symptomatology could readily be traced.

The *primary pathology* occurs in three sites, namely (1) the skin, (2) the lungs and (3) the wall of the small intestine.

FIG 228 —Experimental hookworm infection, showing swelling of wrist and tendons of hand and vesicle formation Second day (After Claude A Smith in Dock and Bass, Hookworm Disease, Courtesy of C. V. Mosby Company.)

1 *The Skin.*—At the time of infection the lesions produced in the skin, as the filariform larvæ effect an entry into the body, give rise to *hookworm dermatitis*, or "ground-itch." Ashford (1911) described this dermatitis in infection with *Necator americanus* (Fig. 228) as first an intense itching and burning; then edema and erythema; then a papular eruption ending in vesicles, usually between the toes, or on the lateral or dorsal surfaces of the feet. Some patients subsequently experience an urticarial rash; many have a secondary pyogenic infection at the site of exposure. Out of 19,000 hookworm patients in Puerto Rico, Ashford found that 96 per cent gave a history of initial dermatitis. On the other hand, Fülleborn (1930) has found that "ground itch" is not common in infections with *Ancylostoma duodenale.*

For a consideration of "*creeping eruption,*" consult pp. 435–437.

2. *The Lungs.*—Following their arrival from the skin in the pulmonary arterioles the migrating larvæ bore their way out of the pulmonary capil-

laries into the air sacs, producing minute hemorrhages, with clotting and the development of new hemorrhages below the first puncture wounds. This results in the infiltration of leukocytes, later of fibroblasts, into the alveoli and bronchioles, ending in fibrous scars and emphysema. If the invasion and migration of the larvæ is massive, lobular consolidation and bronchial pneumonitis may be produced.

3. *The Intestine.*—As soon as the adolescent worms in the small bowel develop a temporary mouth capsule, (*i. e.*, during the last larval stage), they attach themselves to the villi, and by suction and lysis produce erosion of the mucosa and stroma of the villi. This occasions extravasation of blood from the intestinal capillaries. Much of this blood is pumped through the worm's gut and excreted through its anus. This superficial destruction of the bowel wall, with hemorrhage, is continued when the worms acquire permanent mouth capsules, so that by the time they begin to lay eggs the intestinal lesions are well initiated. From time to time the worms abandon the old, unprofitable sites and attach themselves to new locations. The abandoned sites continue for some time to ooze blood and serum, and allow

[illegible]

to the worm burden and increases the amount of intestinal pathology.

Within thirty to sixty days after a massive exposure to infection the characteristic *symptoms*, both objective and subjective, make their appearance. Infected individuals may be grouped into (*a*) acute cases, (*b*) chronic cases and (*c*) symptomless cases.

(*a*) *Acute Cases.*—These patients have been exposed to single, massive infections. About 30 to 60 days after exposure, they develop prodromal symptoms of nausea, headache, lethargy and an irritating cough. This stage is soon followed by one with severe colicky pains in the pit of the stomach, flatulence and a diarrhea or a dysentery in which the stool is viscous and reddish black; in spite of a fair appetite there is considerable loss in weight and strength, dyspnea, dizziness and marked pallor.

(*b*) *Chronic Cases.*—In *moderately light infections* the patient seeks relief from dyspepsia and malaise. He experiences epigastric burning and flatulence, has an abnormally large appetite, gastralgia, and dyspnea on slight exertion. His abdomen is painful on pressure. His skin is sallow. He is nervous, "run down" and is not qualified for heavy labor. *With a somewhat heavier worm burden* the patient's food ferments, enteralgia is persistent, he has alternating diarrhea and constipation, he experiences dyspnea, precordial pains and palpitation of the heart. His nutritional balance is seriously disturbed. He is listless and expressionless, has puffy, pallid facies, flabby muscles and is weak-kneed. He has a diminished patellar reflex; his feet and hands tinge and burn and "go to sleep" easily. His skin becomes dry and harsh. He experiences mental confusion. In men there may be partial impotence, in women amenorrhea; in children there is characteristically both physical and sexual stunting (Figs. 229, 230). The hemoglobin percentage is 60 to 30. He is not fit for labor of any kind. Blackie (1946) considers hookworm responsible for "famine lassitude" observed among natives in Northern Rhodesia. In this region in times of

famine the capacity for work diminishes out of all proportion to the degree of malnutrition which exists. *In severe cases* the anemia is profound, with the hemoglobin percentage below 30. There is marked edema of the face, and the lips are ashen. If the hemoglobin is reduced below 20 per cent, a macrocytic anemia, with megaloblasts and myelocytes in the blood stream, may develop. His feet and ankles become puffy and anasarca frequently develops. His appetite for food is lost except for bulky material to fill his stomach and bowels, hence the syndrome of *geophagia*. He has a fetid

FIG. 229

FIG 230

FIGS 229 and 230.—Clinical cases of hookworm infection; Fig 229, subject aged twenty-two years (After Dock and Bass, Hookworm Disease, Courtesy of C. V. Mosby Company.) FIG 230.—Boy aged fourteen years. (After Stiles in Dock and Bass, Hookworm Disease, Courtesy of C V. Mosby Company.)

diarrhea alternating at times with constipation. Frequently there is extreme flatulence, sometimes abdominal ascites. There is complete mental apathy and confusion, and there may be melancholia or acute mania. The patient is persistently cold, even in hot climates. Unless given supportive and specific relief, he succumbs to a choleric diarrhea or heart failure.

(c) *Symptomless Cases.*—These patients usually harbor fewer than 50 worms, but on a maintained nourishing diet, with adequate iron, several hundred worms may be present without appreciable symptoms.

In more recent hookworm investigations, undertaken to evaluate both

the clinical and public health aspects of the disease, the individual and group significance of the infection has been measured by determining the number of hookworm eggs present in one cc. (roughly one Gm.) of formed stool. The rationale consists in the knowledge that the severity of the infection is proportional to the amount of blood mechanically lost day by day as a result of the activity of the hookworms attached to the wall of the small intestine, and this, in turn, is correlated with the number of worms present. Thus, (1) *heavy infection* (almost invariably of clinical grade) is defined as one in which more than 11,100 eggs occur in one cc. of stool; (2) *moderate infection* (not necessarily of clinical grade), from 2100 to 11,099 eggs, and (3) *light infection* (seldom of clinical grade), fewer than 2099 eggs (Scott, 1945).

It is well established that a primary infection provides considerable immunity to subsequent exposures, while an adequate, well-balanced diet, containing iron and other minerals as well as proteins and vitamin A, may compensate for appreciable blood loss

As a result of the mechanical loss of blood from the small bowel wall in patients with moderate to severe hookworm disease, the hematopoietic mechanism is unable to compensate for the loss in number of erythrocytes

c-

r-

istic of this disease is usually, but not always, correlated with the number of worms harbored It is believed that *Necator* causes less disturbance than *Ancylostoma*. Human ancylostomes have been estimated as capable of removing about 0.67 cc. or more of blood *per* worm *per diem*. While this is probably true for worms which have just become established in the bowel, it is likely that older worms produce a considerably smaller blood loss, possibly not more than 0.1 cc. *per* worm daily The experimental studies of Foster and Landsberg (1934) and the clinical studies of Rhoads, Castle, Payne and Lawson (1934) have convincingly demonstrated that the intestinal hemorrhage produced by hookworms results in the development of a microcytic, hypochromic anemia.

Yokogawa (1937) has found, in 4 series of human experimental infections with hookworms, that the anemia begins to appear in ten to twenty weeks after exposure, and increases with time. During the initial period of infection a pronounced leukocytosis (up to 17,000 white cells) occurs, with a predominant eosinophilia (as high as 55 per cent in some patients). The hypereosinophilia may persist for weeks afterwards, when the total leukocyte count has returned to normal and the erythropenia has assumed the significant rôle. Suarez (1933) studied 19 uncomplicated cases of hookworm disease in Puerto Rico. On admission the patients all had a characteristic hypochromic anemia, with an erythrocyte count varying from one to three and a half million cells per cmm. of blood, reticulocyte count negative or subnormal, a low mean corpuscular volume, a low mean corpuscular hemoglobin, a leukocyte count from 5200 to 10,000 per cmm. of blood, and 2 to 15 per cent eosinophilia. There was no correlation between

, and no signifi-

ood cholesterol,

Although the mechanical loss of blood from the bowel wall (as a result of the pumping action of the hookworms attached to the mucosa and to seepage from the ulcerated lesions which they produce), is most probably the fundamental cause of the hookworm syndrome, this information fails to tell the entire story. In the Philippines Leach *et al.* (1923) discovered some patients who harbored more than a thousand worms and yet showed no serious effects of their worm burden. In other patients, who were parasitized with only a few worms, there was evidence of serious illness. The most important predisposing factor is *chronic malnutrition*, especially in races whose diet is poor in animal proteins and iron. These semi-starved individuals are the ones most commonly exposed to infection, and their nutritional maladjustment both invites and permits a sustained heavy hookworm infection. By way of contrast, even without the benefit of specific therapy, the administration of a balanced, nourishing diet, supplemented with iron, corrects the anemia (Rhoads, Castle, Payne and Lawson, 1934).

Since protein deficiency is a very important contributing factor to the synthesis of hemoglobin (*i. e.*, about 96 per cent of the hemoglobin molecule is derived from dietary protein), even with an adequate intake of absorbable iron anemia may develop and persist if the plasma protein level is subnormal. This is frequently the situation in hookworm belts, where the food consists of an excess of carbohydrates and an insufficient amount of good quality proteins. Moreover, the low plasma protein level contributes appreciably to the edema of malnutrition so frequently observed in areas where hookworm disease is hyp
have been emphasized anew by
hookworm disease and its control in the Southern

Occasionally the blood picture in severe hookworm infection simulates a primary anemia, with the hemoglobin index above unity (Ashford, 1911, Silveira and de Moura Campos, 1937). This may result from a prolonged mechanical loss of blood, or it may develop in individuals with a constitutional predisposition to a primary anemia.

Porter (1937) has demonstrated that in chronic hookworm disease the following physiological adjustments tend to compensate for the anemia. There is an increased vital capacity of the lungs, even in excess of that of natives of high altitudes, and a tissue tolerance for oxygen want. Diastolic blood pressure may be normal but the systolic pressure is reduced, demonstrating that there is no "circulatory compensation for a reduced oxygen-carrying capacity of the blood." The skin pallor is a sign of reduced peripheral circulation as well as Hb deficiency, to meet the more essential demand for greater volume of blood in the vital organs.

In areas where hookworm disease is common, there is not only a tendency to physical, sexual and mental retardation in children (*vide supra*), but even in child-birth the disease may take a tremendous toll. Wickramasuriya (1935) reckons this disease in India to be a more serious complication of
pregnanc ... lampsia and puerperal sepsis.
In his st
90 per cent
nancy, their average blood urea was increased from

cent and their renal function correspondingly lowered. In these patients cardiac shock constituted the most common immediate cause of death.

In addition to the general picture of severe and continued hookworm disease which has thus far been presented, it is important to note that there is not infrequently an associated nephrosis, with albuminuria, hypercholesterolemia and hypoproteinemia, all of which usually result from the low and qualitatively poor dietary protein. Moreover, the symptoms of lethargy, geophagia, impotence, stupidity and decrease in patellar reflexes, and especially morbid paresthesias and blurred vision suggest the intoxicative effect of the disease on the central nervous system (Chalgren and Baker, 1946).

Bonne (1935, 1937) has reported five autopsy cases in which *A. braziliense* eggs, larvæ and adults were present in the submucosa of the jejunum, with marked leukocytic infiltration (primarily eosinophils), and with considerable local tissue destruction. In one patient peritonitis had developed following perforation of the jejunal wall.

Diagnosis.—This is based on finding the characteristic hookworm eggs in the feces. Persons suffering from moderate or severe hookworm disease can almost invariably be diagnosed by microscopic examination of unconcentrated fecal films. Although concentration technics (*vide* pp 539) greatly increase the yield of eggs from stools of lightly infected individuals or population groups, the discovery of many eggs in a concentrate is apt to produce an overemphasis on the clinical significance of the diagnosis Whatever technic is employed in evaluating the severity (*i. e.*, worm burden) in the individual hookworm patient or in a community, it must be borne in mind that, on the average, fewer than 2000 eggs per cc of formed stool indicate a light infection, which is seldom of clinical grade; that a moderate worm burden, in part clinically important, is correlated with an egg count ranging between approximately 2000 and 11,000, and that an egg count in excess of 11,000 is almost always clinically significant For

shape of *Ancylostoma* and *Necator* eggs, in practical diagnosis they are difficult to differentiate. *Strongyloides* eggs, which are similar in appearance but slightly smaller (50 to 58 by 30 to 34 μ), are evacuated only after purgation, or in patients with a persistent watery diarrhea The eggs of the several species of *Trichostrongylus* are larger (73 to 80 by 40 to 46 μ) and have more elliptical ends, but may be confused with hookworm eggs by inexperienced diagnosticians.

"CREEPING ERUPTION"

Biological Data.—Various clinicians in the Southern United States, particularly in Florida and Texas, have from time to time observed cases of so-called "creeping eruption," believed to have been due to fly larvæ. Extensive observations and investigations by Kirby-Smith (1917–1927), and by Kirby-Smith, Dove and White (1926, 1927) in the vicinity of Jacksonville, Florida, where the disease is a serious and extensive clinical entity, have resulted in the discovery that the etiological agent is the filari-

form larva of *Ancylostoma braziliense.* The infection is usually contracted after contact of exposed parts of the body wit

moist, warm months of the year.

Although isolated instances of "creeping eruption," due to cutaneous invasion with this larva, or the infective-stage larvæ of other hookworms, have been reported from areas outside the coastal, sandy regions of the Southeastern United States, as, for example, on the bathing beaches of Matinhos and Ilha do Mel, Paraná, and those of São Paulo State, Brazil, the strains to which man in exposed in South America, Africa and the Orient are apparently better adapted to man and, after penetrating the deeper layers of the skin, proceed to normal development in the small bowel. Furthermore, Africa (1932) suggests that the vitamin content of the food may contribute to the type of infection produced in different peoples.

FIG. 231.—The early lesion of "creeping eruption" due to cutaneous migration of *Ancylostoma braziliense*, infective-stage (filariform) larvæ. The circle indicates the site of the worm at the blind end of the tunnel. (After Kirby-Smith, South. Med. Jour.)

The cattle hookworm, as a causative agent of "c stage larva of this nemat into the skin and migratic tissues parallel *A. braziliense.*

Clinical Data.—At the point of invasion of the skin a reddish, itchy papule develops. Within two or three days the "eruption" consists of a linear, tortuous or serpiginous subepithelial tunnel, produced by the larvæ migrating within the skin. (Fig. 231.) It is accompanied by intense itching, which frequently provokes scratching on the part of the patient and leads to secondary infection. The lesion first develops as a narrow erythematous track along the path traversed by the worm. Soon a slightly elevated line can be palpated; this line becomes vesicular and the surface of the abandoned portion of the channel becomes dry and crusty. The larva migrates from a fraction of an inch to several inches each day. Such lesions may be present on every part of the body (Fig. 232), although invasion of the larvæ most commonly occurs on the hands and feet. The

tunnel is within the *stratum germinativum* and usually has the *corium* as a floor and the *stratum granulosum* as a roof. Local eosinophilia and round-cell infiltration may be present in the immediate vicinity of the lesion. The migration of the larva may continue for several days or even weeks. Its final fate has not been demonstrated, although Fülleborn (1931) described a wandering nematode larva, possibly of a species of hookworm, which persisted on the hand for twenty-four years.

The lesion produces an itchy sensation, which is almost intolerable to some patients, causing insomnia, loss of appetite and, in certain extreme cases, loss of weight and vitality.

"Creeping eruption" resulting from invasion of the skin with hookworm larvæ requires differentiation from that produced by the spiruroid nematode, *Gnathostoma spinigerum* (*vide* pp. 487), as well as the more frequent cutaneous myiasis, occasioned by the maggots (larvæ) of flies, especially of the genera *Gasterophilus* and *Hypoderma* (See Faust, in Craig and Faust, 1945, pp. 689, 693–698.)

FIG. 232 —Late stage of "creeping eruption" of *A braziliense* origin (After Kirby-Smith, in Stitt's Diagnostics, courtesy of P Blakiston's Son & Co)

Therapeusis.—Successful treatment of "creeping eruption" produced by hookworm larvæ has been effected by the local application of ethyl acetate in collodion, local freezing with ethyl chloride spray or carbon dioxide snow, and by radiotherapy. There is no evidence that systemic administration of tartar emetic, fuadin, neostibosan or oxyphenarsine hydrochloride has any specific action on the worms Kirby-Smith (1935), on the basis of his extensive clinical experience with this infection, recommends ethyl chloride spray as the treatment of choice. Secondarily infected lesions should be treated with bactericidal or fungicidal agents before specific therapeusis is instituted.

patient with a minimum toxic effect on the patient. Various drugs have been tested but relatively few have been found to be efficient. Caius and

... comparative efficiency of more than seventy drugs Darling and his colleagues (1920) in the Malay States, Java and the Fiji Islands carried out clinical tests on thymol and oil of chenopodium, both of which they found promising. Carbon tetrachloride, tetrachlorethylene and hexylresorcinol were all assayed in the pharmaceutical laboratory before they were used clinically.

General Management.—Since patients with hookworm disease are suffering from anemia and frequently in highly endemic areas also from inadequate dietary proteins, it is essential to rectify these deficiencies. If the anemia is severe, wherever possible the patient should be hospitalized and two or three transfusions of whole blood administered. This will not only temporarily increase the circulating red blood corpuscles and reduce the oxygen want but will similarly partly relieve the deficit in plasma protein. As soon as possible the patient should be given a well-balanced diet, with adequate carbohydrates to care for metabolic needs and rich proteins to repair the hypoproteinemia. Possibly protein concentrates should be considered as supplement to the dietary protein. Iron must also be fed. Ferrous sulfate is most satisfactory and its taste can be partly concealed by mixing it with flour. Cruz and de Mello (1945) recommend ferrous sulfate in the amount of 1 Gm. per day until the hemoglobin level is raised to 10–11 Gms. per cent, then 0.5 Gm. daily for 80 days, followed by 0.25 Gm. for another 80 days. Usually in one to two weeks after instituting general therapy the patient is much improved. Specific therapy should be undertaken as early as the patients' condition warrants.

Thymol.—This drug has been used for eradicating human hookworms since 1879, and soon thereafter became generally adopted for this purpose, although it was not critically assaye[illegible]
(1919) With a [illegible]
cent worm remo[illegible]
Ashford and Igaravidez (1911) obtained 68.8 per cent cures. Chopra (1936) recommends for an adult two or three divided doses of 1 to 2 Gms. (15 to 30 grains) each, of the powdered or finely granular product, mixed with lactose or sodium bicarbonate, and followed within two hours by saline purgation.

Even under careful management of the patient thymol is toxic. It irritates mucous membranes; it first stimulates, then depresses the central nervous system. It produces headache, vertigo, tinnitus, and subnormal temperature. It irritates the kidneys and frequently produces albuminuria. When given in excess, it may result in collapse.

Today thymol is less frequently used than it was even a decade ago. It has been generally superseded by anthelmintics which are more efficient or which have a

the immediate supervision of a physician who knows its toxic properties. Today oil of chenopodium is not used for hookworm eradication, except in combination with carbon tetrachloride or tetrachlorethylene.

Carbon Tetrachloride (CCl_4) —Carbon tetrachloride has been known to have anesthetic powers for more than three-quarters of a century, but its use as a vermicide was not demonstrated until Hall made a study of its effect on the strongyles of domestic animals. The results he obtained were so successful that in 1921 he called the attention of the medical profession to the possibility of its use in human hookworm therapy. Following this Leach (1922) in Ceylon and Lambert (1924) in Fiji made careful preliminary investigations on its potency and its effect on patients Leach used up to 12 cc. of the drug with no untoward effects and, in cases of prisoners to be hanged, which were treated and later came to autopsy, no hookworms were found, although *Enterobius* and *Trichocephalus* still remained attached to the cecal wall In Lambert's preliminary tests 96 to 98 per cent efficiency was obtained by the administration of 3 cc. of CCl_4. He secured 85 per cent cures from the first dosage. Following these tests, Lambert treated more than 100,000 cases, and with the single-treatment method reduced the infection from nearly 100 per cent to 9 per cent without the loss of a single case. The cost of the treatment was less than 9 cents gold per patient. The dosage given was 0 2 cc for each year of age up to fifteen years, when the adult dosage of 3 to 4 cc was administered The drug was placed on a tablespoon, floated on water and swallowed. After preliminary tests it was found that routine $MgSO_4$ purgation three hours after the drug had been administered removed practically all of the after-effects Leach had similar success

marvelous " However, certain of their cases had toxic after-effects, believed by them to be due to the drug (*i e*, fatty degeneration of the liver), but these cases were chronic alcoholics This led them to try out smaller dosages (1 to 1 5 cc) which they found unsatisfactory They concluded that 3 cc. is the maximum safe dose for an adult They recommended the use of the drug as follows (1) light supper, (2) no breakfast; (3) 7 A M CCl_4 (c p) given in doses of 2 minims per year of age up to the maximum amount, administered either in gelatin capsules or floated

produces fatty degeneration of the liver cells, with jaundice, vomiting and bilirubinemia Once in the general circulation, it depresses the circulation and the heart tone, causes giddiness and frequently drowsiness In case there is a low serum calcium, there may be tetanic convulsions, cloudy swelling and fatty degeneration of the kidneys Deaths following administration of this drug have almost without exception been in chronic alcoholics, vagabonds or persons with hepatic and

carbon tetrachloride treatment alone The most efficient, and at the same time the

safest, combination of these anthelmintics, together with pre-treatment preparation and post-treatment care, is as follows (adult dose): (1) light supper; (2) sodium sulfate (Glauber salts) purge (one-half ounce or 15 Gm. in a glass of water) before retiring; (3) no breakfast; (4) 2.7 cc. CCl_4 (c. p.) and 0.3 cc. oil of chenopodium, floated on a tablespoon; (5) two to three hours later, sodium sulfate purge; and (6) light noon meal.

Tetrachlorethylene (C_2Cl_4)—This drug was recommended to the medical profession for trial by Hall and Shillinger (1925), who found it to be very efficient and essentially non-toxic in removing hookworms in dogs. It has been investigated pharmacologically by Lamson, Brown and Ward (1932), who found that it does not irritate mucous membranes, and produces no appreciable damage to the liver parenchyma or glomeruli of the kidneys. Shapiro and Stoll (1927) estimated that a dose of 3 cc. to an adult patient removed 93 per cent of the hookworms; Kendrick (1929) gave it an 89.8 per cent worm removal rating; while Pessôa and Pascale (1937), using 4 cc. doses, obtained a 95 per cent removal of necators. It has been used on hundreds of thousands of patients, with not more than three or four deaths and characteristically no serious sequelæ. The only ill-effects noted following its administration have been transient headache and vertigo.

The recommended dosage of tetrachlorethylene is 3 cc. for an adult, 3 minims per year of age for children. Preferably the patient should abstain from taking alcohol or absorbable fats for two days before treatment, and on the preceding night eat only a light supper and take a Glauber salts (Na_2SO_4) purge (one-half ounce or 15 Gm. in a glass of water). On the

allowed until a copious evacuation of the bowels has been obtained. Rest in bed during treatment is indicated.

Contraindications.—There are no known contraindications to prescribing this drug, but in administering the drug to children it is advisable to keep them in bed during the hours of treatment. Only the fresh preparation should be employed, since the preparation in old globules or the drug when exposed to the air for more than a brief period tends to decompose, with the formation of phosgene gas.

Crystoids Anthelmintic (*Hexylresorcinol, Caprokol*).—This drug has a relatively high rate of efficiency in evacuating hookworms. In therapeutic amounts of 1 Gm. Lamson, Brown, Robbins and Ward (1932) obtained 80 to 89 per cent worm removal (necators) and 42 per cent cures, and with two consecutive daily doses of 0.6 Gm. each, 85 to 97 per cent worm removal and 60 to 88 per cent cures. The patients, mostly school children, were given saline purgation the night before treatment, took the drug on an empty stomach in the morning, fasted until noon and were given post-treatment purgation. In the author's experience this drug has about a 75 per cent worm removal rate. However, in spite of its lower efficiency for evacuation of hookworms, when compared with the drugs considered above, it has the advantage of high efficiency in ascariasis and may be taken without interfering with daily routine. It is the drug of choice in combined hookworm and *Ascaris* infections. The drug is available in 0.1 and 0.2 Gm. hard gelatin capsules. The capsules must not be chewed or crushed before swallowing and must be taken on a fasting stomach.

Mass Therapy.—The recommendations which have been made above for the evacuation of hookworms, together with supportive treatment in hookworm disease, are intended for use in individuals or small groups, who can be adequately diagnosed and treated in infirmaries. For tropical villages, or estates and plantations having large groups of laborers, but with limited facilities for hospitalization, these recommendations may not be practicable. In heavily inf

(Darling, 1920,

Lane technic (pp

entire community is subjected to a single treatment with an anthelmintic potent enough to eliminate the majority of the hookworms but sufficiently safe to prevent serious sequelæ. Tetrachlorethylene (because of its low toxicity) may be given in therapeutic doses, either accompanied or followed within an hour by Glauber salts (sodium sulfate) or Epsom salts (magnesium sulfate) purgation. However, as Chandler (1929) has pointed out, in a heavily infected population, the soil is for some time afterwards a source for acquiring reinfection. Thus, several mass treatments, spaced a few months apart and accompanied by the establishment and use of the appropriate type of sanitary latrine, are needed to reduce hookworm infection in the community to a clinically negligible status.

Prognosis.—Except for the relatively few individuals who come to the clinic *in extremis*, prognosis is good to excellent, provided a nutritious, balanced diet, with iron, is secured and specific therapeusis is carried out.

Control.—As Scott (1946) has pointed out, well-nourished individuals have enough resistance to prevent the establishment in the intestine of hookworms in sufficient numbers to cause appreciable anemia. It is the malnourished persons, who have lost the protective balance, in whom extensive or repeated exposure produces a heavy hookworm burden, with a drain on the hematopoietic system already near its maximum compensatory limit. The degree of anemia should be determined by Hb determina-

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the sanitary disposition of night-soil; and (3) treatment of infected individuals. The first and the third methods tend to reduce the infection in man, while the second and third reduce the source of infection

In the United States and similar areas of infection in Europe the program for prevention may be stated as follows.

1. Every person, who can possibly afford to do so, should wear shoes the year round, and miners in infected areas should wear leather gloves and other body-covering.

2. Every person should use either toilets connected with sewers, or sanitary latrines Sewers are in use in the large cities of the Southern United States and are known to constitute a very important agency in reducing all forms of intestinal diseases They can and should be extended

into the smaller cities and towns. Sanitary cesspits can be utilized in the homes of persons of moderate means, but there is still left a moiety of the population unsupplied with such improved sanitary conveniences. Furthermore, it is just this part of the population that is most seriously affected. Sanitary latrines have been talked about and devised ever since the hookworm problem has been appreciated by sanitarians, but in practice they have usually been a failure, either through faults in the type of construction or because of expense of such a building, or through inertia on the part of individuals to use and maintain them. For the rural community a closed-back latrine, with a deep pit and house set upon the pit, is desirable, so as to prevent animals from grubbing into the hole. In places where poor, insanitary and uncomfortable outhouses are provided, the individual frequently chooses a place

this may meet the tempor...

the most intense bed for hookworm larvæ to breed. In many tropical countries the bore...

to be much more s...

should be studied

be m...

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built and giving administrative officers power to enforce such regulations

3. Anthelmintic medication should be carried out for individuals, small groups or larger populations whenever stool examination demonstrates the need based on incidence of infection and worm burden. This latter determination is possible only by means of quantitative egg counts. Both direct fecal films and concentration technics are essential, the latter to detect light infections (Keller and Leathers, 1940).

4. Careful attention should be given to the diets of the hookworm ... Although diet may be adequate in calories, almost invariably ...

iron in concentrated form, as ferrous sulfate.

5. The public should be educated by popular lectures and cinemas as to the causes, losses due to, and methods of practical control of hookworm disease.

6. Fund must be made available to make periodic re-surveys to check on

factors involving ...

hookworm control. The greatest success has been attained by ... interest and support of plantation owners (tea, coffee, rubber, *etc.*), and in proving to them that hookworm prevention is of positive economic value. This work has been carried on along the following lines:

a. Constructing of sanitary outhouses or *bored-hole* latrines near "coolie-lines."

b. Treatment of infected individuals.

...

of agriculture, an additional factor is involved, namely, the danger from conservation of the feces and spreading of it on the soil Oldt (1926) has shown that the
a 12 per cent st
embryos within
important in view of the fact that the day is not far off when Western as well as Oriental nations will have to return all fertilizer, including human dejecta, to the soil.

Mass Treatment.—"By mass treatment is meant the administration of vermicide to large or small bodies of people—all the inhabitants of a com-

mass treatment are: (1) The difficulty of identifying and locating individuals; (2) the reduction of soil pollution resulting from the treatment; (3) the psychology of the "follow the crowd" instinct, and (4) the bringing of larger groups under treatment.

In the Southern United States hookworm disease is no longer the extensive clinical or public health problem which it was at the beginning of the century, when Stiles initiated the hookworm surveys. There is still relatively widespread infection, with areas of hyperendemicity in southeastern Georgia, parts of Florida, Alabama, Mississippi, Louisiana, and in eastern Texas. In the Tropics and some Oriental countries extensive hookworm infection, frequently with an average heavy hookworm burden in the individual, persists, in spite of the prolonged intelligent attack on the problem by the International Health Division of the Rockefeller Foundation and by the Public Health Departments of local governments. Only by persistent attack on the problem can hookworm be eliminated as a major menace to health in warm countries

Superfamily Trichostrongyloidea Cram, 1927

This superfamily is composed of strongylate nematodes in which the buccal capsule is lacking or only rudimentary. They are long, attenuate worms, with a conspicuous bursa copulatrix. All of the human parasites in this group belong to the type family **Trichostrongylidæ** Leiper, 1912, the species of which are characterized by lacking a buccal capsule and dental apparatus, and by having a large bursa with well-developed rays. These species are commonly parasitic in the digestive tract of ruminants and, except for *Trichostrongylus orientalis*, are less commonly parasites of man than of herbivorous mammals. All of the members of this family with known life histories require only one host, but have a free larval period. Species belonging to the genera *Trichostrongylus*, *Ostertagia*, *Hæmonchus* and *Mecistocirrus* have been reported as parasites of man.

Genus Trichostrongylus Looss, 1905

(genus from θρίξ, thread, and στρογγύλος, round)

Stoll (1947) has estimated human infection with the several species of

Trichostrongylus to be 5.5 millions, with 1.0 million assigned to the U.S.S.R., 4.5 millions to Asia and elsewhere incidental.

Trichostrongylus colubriformis (Giles, 1892) Ransom, 1911. (The serpentine trichostrongyle, producing trichostrongylosis colubriformis.)

Synonyms.—*Strongylus colubriformis* Giles, 1892; *Strongylus instabilis* Railliet, 1893; *Strongylus subtilis* Looss, 1895; *Strongylus retortæformis* Zeder, 1800 *pro parte*; *Trichostrongylus subtilis* Looss, 1905; *Trichostrongylus instabilis* (Railliet, 1893) Looss, 1905; *Trichostrongylus delicatus* Hall, 1916.

Biological and Geographical Data.—*Trichostrongylus colubriformis* is a small, slender worm, with a reddish or creamy color when alive. It has been recorded from the duodenum and fourth stomach of several ruminants, including the domestic sheep, Dorcas gazelle (*Gazella dorcas*), Grant's gazelle (*G. granti*), the Arabian and the Bactrian camel, the goat, prong-horned antelope (*Antilocapra americana*), the sable antelope

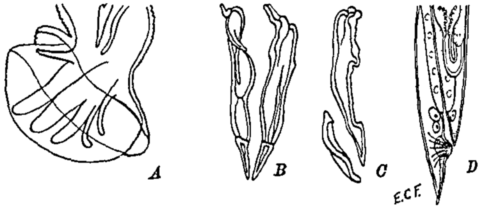


FIG. 233 —*Trichostrongylus colubriformis*. *A*, bursa of male worm, × 250; *B*, *C*, copulatory spicules, ventral and profile views, × 250; *D*, posterior end of female worm, × 150 (After Looss, in Centralblatt f. Bakteriologie u Parasitenkunde.)

(*Hippotragus niger*), the roe deer and the bharal (*Ovis nahura*). It has also been found in the small intestine of the Arabian baboon (*Papio hamadryas*), the Java ape (*Macaca cynomolgus*), squirrels (*Sciurus aberti mimus* and *S. carolinensis*), the rabbit (in Java) and has been obtained as a human infection in Egypt (Looss), India (Lane, Chandler), Armenia (Kalantarian), Java (Lie Kian Joe) and the Atherton tableland of Australia. A single male specimen of this species has been diagnosed by the author from a surgical appendix of a New Orleans patient (1937).

In post-mortem studies conducted in Java Lie Kian Joe (1941) found 40 per cent incidence in 119 Indonesians and 19 per cent in 32 Chinese, although the number of worms recovered was consistently small (73 maximum). However, in one necropsy from an insane hospital more than 5000 *T. colubriformis* and many hookworms were obtained. From five years of age to fifty years or more in the Indonesian population the incidence of human infection remains relatively constant (Lie Kian Joe, 1947).

The male worm has a length measurement of 4 to 5.5 mm. and a greatest diameter of 80 μ in the prebursal region. The head measures only about 10 μ in cross-section. The bursa is bilobed (Fig. 233 *A*), with the externo-

lateral ray usually broader than the other rays, and the postero-lateral small and closer to the externo-dorsal than the latter is to the dorsal. The dorsal ray is bifid, each branch having a double point. The spicules (Fig. 233 *B*, *C*) measure 135 to 145 μ long, while the gubernaculum (Fig 233 *C*, left) is slender, of a bright yellowish-brown color, and has a length of 70 μ The terminal portion of the spicules is fairly sharp, with a definite but not high elevation.

The female worm measures 5 to 6 mm. in length by 80 μ in diameter at the level of the vulva, with a gradual tapering towards the anus (Fig. 233 *D*). The distance between the anus and the caudal extremity ranges from 55 to 70 μ. The vulva is longitudinally elongated, measuring 50 to 55 μ The eggs are oval-elliptical, transparent, and measure 73 to 80 μ in length by 40 to 43 μ in lesser diameter. They are usually discharged in the morula stage of embryonation and under favorable conditions of warmth and moisture may hatch in twenty-four hours, or may survive long cold

anterior portion, a constricted region behind the esophageal nerve ring, and a typical, posterior bulbous swelling. They have a distinct dorsal bend at the level of the anus. The attenuate postanal region terminates in a minute knob. There are three free-living larval stages, with two ecdyses The semi-filariform third larval stage, which has a length of about 690 μ, and has a slight serpentine curve to its body, may develop within 60 hours after hatching has occurred but more often requires 96 hours. Its tail is bluntly rounded but is provided with a minute, sharp terminal process (as contrasted with the sharply pointed tail of hookworm larvæ and the forked caudal terminus of *Strongyloides* larvæ of this same stage). This infective-stage larva of *Trichostrongylus* is very resistant to desiccation (Mönnig, 1927).

Normally this larva is ingested by its host, along with grass, and on reaching the small intestine casts its sheath (third ecdysis) and burrows into the intestinal muco
lumen and, after a four
end into the intestinal .
period requires about three weeks, as determined in goats and in man (Lie Kian Joe, 1947).

Epidemiology.—Human infection is incidental to that in herbivorous mammals, which are reservoirs of the worms. The infective-stage larvæ survive as long as 15 months on pasture lands and withstand severe droughts. Infection is acquired *per os*.

Pathogenesis, Pathology and Symptomatology.—In man the worms occur predominantly at the levels of the duodenum and jejunum but they may extend from the pylorus down through the small intestine. In case large numbers of these worms develop in the human intestine, they may produce a severe secondary anemia, due to the blood-sucking habits of the worms and possibly to toxins which they secrete into the intestinal wall. In light experimental human infections Lie Kian Joe (1947) observed only a transient eosinophilia (maximum, 10 per cent).

Diagnosis.—Upon finding the characteristic ellipsoidal eggs in the feces of a suspected patient. These eggs are much longer and have more pointed ends than hookworm eggs, but the eggs of the several species of *Trichostrongylus* are difficult to differentiate from one another. (See Fig. 237.)

Therapeusis.—Similar to that for hookworm infection. Mönnig (1938) recommends tetrachlorethylene, but it is doubtful if this drug or carbon tetrachloride is as satisfactory for trichostrongylosis as it is for hookworm infection.

Prognosis.—Usually good.

Control.—Man acquires the infection from consumption of raw plant stems and leaves contaminated with the dung of parasitized reservoir hosts, in a medium sufficiently moist during the incubation of the larval stages to permit their development, but possibly very dry at the time accidentally ingested by man. Hence, care not to ingest gross stems or blades in enzoötic foci will probably prevent human infection.

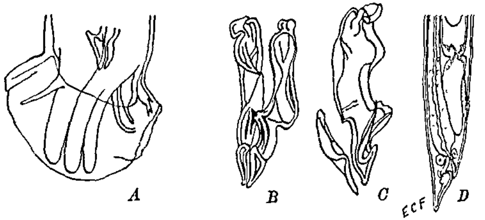


FIG. 234 – *Trichostrongylus probolurus.* *A*, bursa of male worm, × 250, *B*, *C*, copulatory spicules, ventral and profile views, × 250, *D*, posterior end of female worm, × 150 (After Looss, in Centralblatt f Bakteriologie u. Parasitenkunde)

Trichostrongylus probolurus (Railliet, 1896) Looss, 1905.

Synonym.—*Strongylus probolurus* Railliet, 1896.

This species has been found as a natural infection in the duodenum of the domestic sheep, the Dorcas gazelle, the Arabian camel, the Bactrian camel and man in North and East Africa, Europe, Asia, North and South America. The human cases have been reported from the Egyptian fellaheen by Looss (1905), from Armenia by Kalantarian (1927), and from Siberia by Skrjabin and Schultz (1928).

In color, shape, and size th[illegible] *colubriformis*. The latero-ven[illegible] rays (Fig. 234*A*), while the ex[illegible] curves so far dorsad that its t[illegible] ray. The spicules (Fig. 234*B*, [illegible] having a conspicuous [illegible] and relatively thick [illegible] and a sharp angle fa[illegible] low magnification. [illegible] portion of the body of the [illegible]

76 μ long. The transparent ellipsoidal eggs measure 76 to 80 μ in length [illegible] in lesser diameter. (See Fig. 237.)

The life cycle of the worm, symptomatology of the infection and prophylactic aspects are similar to those of *T. colubriformis*.

Trichostrongylus vitrinus Looss, 1905.

se
ta...

relatively more slender and straighter, the ventral and the postero-lateral being conspicuously straight digitate processes. The spicules (Fig 235*B*, *C*) are long (160 to 170 μ); the acuminate points lack the hook-like projection of many species of the genus The slender gubernaculum measures 85 to 95 μ in length The female (Fig. 235*D*) is subcylindrical from the level of the loop of the posterior ovary to the anus, while the post-anal portion becomes reduced to a sharp point with a somewhat ventral curve. The vulva is short and oblique in position, with slight elevation above the surface. The eggs are transparent ellipsoidal objects, measuring 84 to 90 μ in length by 46 to 50 μ in lesser diameter. (See Fig 237)

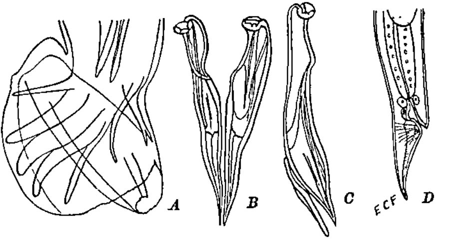


Fig 235.—*Trichostrongylus vitrinus* *A*, bursa of male worm, × 250, *B*, *C*, copulatory spicules, ventral and profile views, × 250, *D*, posterior end of female worm, × 150 (After Looss, in Centralblatt f. Bakteriologie u Parasitenkunde)

The life cycle of the worm, symptomatology of the infection and prophylactic aspects are similar to those of *T. colubriformis*

Trichostrongylus orientalis Jimbo, 1914 (The oriental trichostrongyle, producing trichostrongylosis orientalis.)

Synonym.—*Strongylus subtilis* Looss, 1895 *pro parte*.

Biological and Geographical Data.—This species of *Trichostrongylus* is quite common among the agricultural populations of Japan, Korea and Formosa and is occasionally diagnosed
also found this infection in Armenians.
originally discovered as a human infection.
species in fat-tailed sheep and Bactrian camels in North China. The trichostrongylid originally reported by Ogata, by Ijima, and by Kitamura

and Oishi from human cases in Japan and Korea under the name *Strongylus subtilis* Looss, 1895, is undoubtedly referable to *T. orientalis*. Jimbo records the infection from 219 individuals and from 27 autopsies. In most cases only a few worms were present, exceptionally 50 or more. The common seat of infection was found to be the duodenum, but occasionally worms had wandered into the adjacent portion of the stomach or the jejunum.

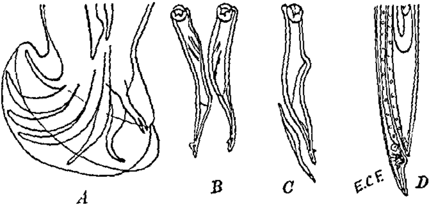


FIG. 236.—*Trichostrongylus orientalis*. *A*, bursa of male worm, × 250; *B*, *C*, copulatory spicules, ventral and profile views, × 250, *D*, posterior end of female worm, × 150 (Original)

The adult worms are grayish-white in color, the males measuring 3.8 to 4.8 mm. and the females 4.9 to 6.7 mm. long. The heads of the males average 7 μ in diameter, and of the females, 9 μ, while the greatest diameter of the former is 72 to 79 μ, and of the latter, 75 to 83 μ.

The bursa (Fig. 236 *A*) is bipartite. The three lateral rays are close to one another, the latero-ventral being the broadest. All three are bowed ventrad, as is also the more slender postero-lat-

two spicules (Fig. 236 *B*, *C*) measure

. There is

h spicule.

n length;

in front view it resembles a pen nib, but in pro-

file view it is spindle-shaped, with a slight bow

end of the female (Fig. 236 *D*)

to the tip of the tail is 65 to 80 μ,

ventral curve. The eggs (Fig. 237) measure 75 to 91 μ, in length by 39 to 47 μ in lesser diameter.

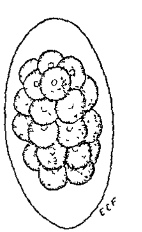


FIG. 237.—Egg of *Trichostrongylus orientalis* × 500. (Original)

The life cycle of this worm is similar to that of *T. colubriformis* (Hasegawa, 1930).

Clinical Data.—The symptoms in mild infections are essentially *nil*. Carbon tetrachloride, as administered in hookworm infection is a semi-specific therapeutic. It is considerably less efficient for trichostrongylosis

than it is for hookworm infection. Man appears to be the common natural host of this species, while other mammals are only incidentally infected.

Other Species of Trichostrongylus Reported From Man.—The following additional species of *Trichostrongylus* have been reported as incidental parasites of man: *T. instabilis* (Railliet, 1893) Looss, 1905, reported from Armenia by Kalantarian (1934) and from Siberia by Skrjabin and Schultz (1928); *T. axei* (Cobbold, 1879) Mönnig, 1934 (syn. *T. extenuatus*), reported from Armenia by Kalantarian (1927), from Siberia by Skrjabin and Schultz (1928), from Mauritius by Webb (1937) and from Java by Lie Kian Joe (1941, 1947); *T. skrjabini* Kalantarian, 1928, reported from Armenia by Kalantarian (1934). In addition, unspecified specimens of *Trichostrongylus* have been obtained from human cases in Tunis (Espie, 1931), from Europeans in the Belgian Congo (Rodhain, 1932), in natives of Southern Rhodesia (Sandground, 1929), from a native of Chile (Ottmar, 1939), from a Greek in the United States (Tsuchiya and Reller, 1944) and from natives of Hawaii and the Fiji Islands.

Furthermore, Heide (personal communication, 1939) found *Tricho-*
antonese soldiers.
by inexperienced
bon tetrachloride
are required to eradicate the worms, a diagnosis of "hookworm disease," followed by CCl_4 therapy, may give a wholly wrong idea as to the efficiency of this drug in hookworm infection.

Watson (1946) has suggested that the occasional infection with *Trichostrongylus* diagnosed by recovery of eggs in the stool may actually be a pseudo-infection, resulting from ingestion of food contaminated with the dung of reservoir hosts loaded with the eggs

Genus Ostertagia Ransom, 1907

(genus named after Robert Ostertag)

These are trichostrongyles with a delicate head and a small buccal cavity; with cervical papillæ. In the male the caudal bursa is provided with two large lateral lobes joined by a small dorsal lobe, the ventral rays are close together; the antero-lateral rays separate the other laterals; the external dorsals develop separately; the dorsal ray is bifurcated at its distal portion, each fork consisting of one or two short rami. The copulatory spicules are equal, short, and terminate in one, two or three points; a gubernaculum may be present or lacking. Prebursal papillæ are present The vulva of the female opens in the posterior fifth of the worm. Members of this genus are oviparous and parasitize herbivorous mammals. The life
'us.
vered a single male
. human necropsy and
O circumcincta (Stadelman, 1894) Ransom, 1907 from another case. He suggests that the infections were most likely incidental and accidental, possibly from eating inadequately cooked abomasum of cattle, sheep or goats containing the nodular stage.

Genus Hæmonchus Cobb, 1898

(genus from αἷμα, blood, and ὄγχος, spear)

Hæmonchus contortus (Rudolphi, 1803) Cobb, 1898. (The sheep wireworm, producing hæmonchiasis.)

Synonyms.—*Strongylus contortus* Rudolphi, 1803; *Strongylus filicollis* Rud. of Molin, 1861; *Strongylus placei* Place, 1893.

Biological and Geographical Data.—This nematode is one of the commonest parasites of domestic sheep throughout the world. It has also been recorded from the goat, the addax, the moose, the prong-horned antelope, the chamois, the American bison, the deer, the roe deer, the mule deer, the bharal, the argali, the Mexican mountain sheep, the Newfoundland caribou, and domestic cattle. De Magalhães has recovered this species once from man in Brazil. On the basis of eggs found in the feces W. S. Sweet (1924) reported the presence of this parasite in three aborigines in Northern Australia.

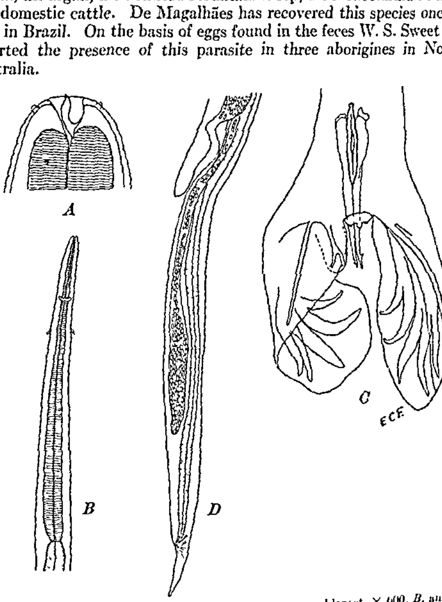


Fig 238.—*Hæmonchus contortus.* *A*, head showing pharyngeal lancet, × 600, *B*, anterior portion of worm showing cervical papillæ and esophagus, × 46, *C*, bursa of male worm, with bursal rays, copulatory spicules and gubernaculum, × 75; *D*, posterior end of female worm, showing vulva and anus, × 24. (After Yorke and Maplestone, Nematode Parasites of Vertebrates, *C*, somewhat modified.)

The worms live attached to the wall of the fourth stomach of the ruminant host, and occasionally to the duodenal mucosa. The buccal cavity in

The males are 10 to 20 mm. long with a maximum thickness of 0.4 mm. and the females, 18 to 30 mm. long by 0.5 mm. in cross-section Anteriorly the body is gradually attenuated. There is an asymmetrically situated dorsal lobe (Fig. 238 *C*) of the bursa copulatrix attached to the left lateral lobe on its inner side near its base. The three lateral rays originate from a common stem, as do the ventro-ventral and the latero-ventral rays. The externo-dorsal is a long, digitate process, that of the left side having its origin close to the base of the common stem of the dorsal ray. The spicules measure 0.3 to 0.5 mm. in length and become gradually attenuated from their point of insertion to their distal tips The tips are provided with minute knobs and a subterminal barb, the barb of the right spicule being slightly larger. The gubernaculum is 200 μ long, flat, fusiform, and has rounded thickened edges

In the female worms the vulva (Fig. 238 *D*) is situated 3 to 4 5 mm. from the caudal extremity. It is protected by a posteriorly projecting linguiform process about 0.5 mm. long. The anus is 0 4 to 0.63 mm. from the tip of the tail. The postanal region is sharply pointed. The eggs are transparent, thin-shelled, ovoidal objects, measuring 75 to 95 μ long by 40 to 50 μ in lesser diameter, and contain incompletely developed larvæ when laid. The life cycle resembles that
third-stage larva appears in .
very resistant to desiccation
stems. Upon ingestion it develops in the abomasum of sheep and other herbivores and begins to lay eggs in eighteen to twenty-one days after exposure has occurred

Glaser and Stoll (1938) have been able to grow the free-living larval stages and the adolescent parasites on bacteria-free media.

Epidemiology.—Pasture and grazing land is kept seeded with this parasite by the droppings of infected animals containing the immature eggs. The first two larval stages require some moisture for their survival, but once the third, ensheathed larva has developed, drought and cold are endured for long periods Upon return of moist conditions, the ensheathed larvæ are revived and crawl upon vegetation, the ingestion of which exposes the grazing animal to infection. Human infection is entirely accidental.

disturbances The infection causes considerable mortality in young animals In man the infection gives rise to a secondary anemia likely to be confused with hookworm anemia Brumpt and Joyeux have shown that the aqueous extract of the worms is hemolytic.

Diagnosis.—Since the eggs are readily confused with those of other strongylate nematodes, it is necessary to obtain specimens of adult worms for specific diagnosis, or to culture the eggs through to the third larval stage.

Therapeusis.—Thymol causes the evacuation of large numbers of the worms. Carbon tetrachloride is not effective in tolerated doses and tetrachlorethylene must be repeatedly administered in large amount to be efficient.

Prognosis.—Relatively poor, because of the relative inefficiency of the available anthelmintics.

Control.—Rotation of crops, so as to obtain uninfected fields for grazing animals, is an effective method of controlling the infection in reservoir hosts. Human beings should refrain from eating uncooked grass or other vegetation in endemic areas, and should thoroughly cleanse the hands after working in infested fields.

Genus Mecistocirrus Railliet and Henry, 1912

(genus from μήκιστος, very long, and *cirrus*, thread)

Mecistocirrus digitatus (v. Linstow, 1906) Neveu-Lemaire, 1914.

[illegible]

of these animals. It has been recorded once from the feces of man in Hongkong, but there is considerable probability that the material in question was not human in origin.

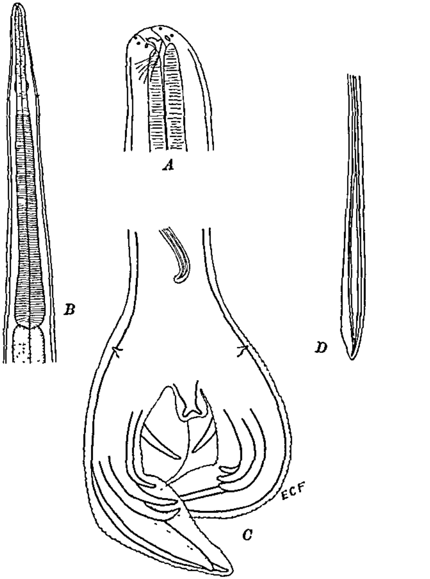
The worms are ivory-colored The males measure 16 to 21 mm. in length by 0.45 mm. in transverse diameter and the females, 19 to 43 mm. in length by 0.5 mm. in diameter. The anterior end is rounded, with six inconspicuous papillæ (Fig. 239*A*). There is a single large pharyngeal lancet present. The cervical papillæ lie in small depressions in the cuticle at the level of the junction of the anterior and second quarters of the long slender esophagus (Fig. 239*B*). In the male there is a pair of prebursal papillæ. [illegible] small dorsal and tw[illegible] are equally large and conspicuous. The ventro-ventral and the extern[illegible] are very slender, and the median- and postero-laterals are intermediate in size. The spicules are long and lanceolate (Fig. 239*D*). The gubernaculum appears to be lacking.

The vulva of the female worm is a prominent transverse slit about 0.3 mm. in front of the anus [illegible] 1.0 ? mm. from the caudal extremity. The tip of the tail is [illegible] measuring 95 to [illegible] the morula stage. The life cycle of the worm is not known but is [illegible] similar to that of the other trichostrongyloid species.

Clinical Data.—The clinical aspects of infection with this species are quite similar [illegible]

Superfamily Metastrongyloidea Lane, 1917

The members of this superfamily are characterized by the absence or *rudimentary condition of the buccal capsule, while the males have a small* bursa with stunted rays, of which the externo-lateral is usually wider and frequently several times the size of the other rays. All species of this group belong to the type family **Metastrongylidæ** Leiper, 1909, which has the characters of the superfamily. The worms live in the respiratory or circulatory system or in the cranial sinuses of mammals. The one species of this



[illegible] Parasites of Vertebrates.)

superfamily recorded from man, *Metastrongylus elongatus*, is a parasite of the lungs.

GENUS METASTRONGYLUS MOLIN, 1861

(genus from μετά, behind, and στρογγύλος, round)

Metastrongylus elongatus (Dujardin, 1845) Railliet and Henry, 1911. (The porcine lung worm, producing metastrongylosis.)

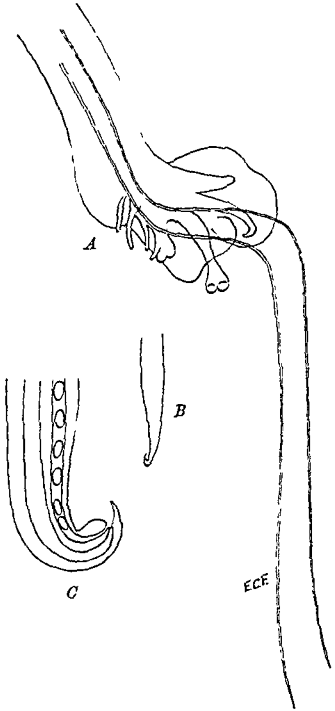


FIG. 240—*Metastrongylus elongatus*. *A*, posterior end of male worm, showing bursa with rays and filiform copulatory spicules, × 75; *B*, hooked end of spicule, greatly enlarged; *C*, posterior end of female worm, showing openings of vulva and anus, × 75 (Original)

Synonyms.—*Gordius pulmonalis apri* Ebel, 1778; *Ascaris apri* Gmelin, 1790; *Fusaria apri* Zeder, 1803, *Strongylus suis* Rudolphi, 1809 *pro parte*, *Strongylus paradoxus* Mehlis, 1931 *pro parte*, *Strongylus elongatus* Dujardin, 1945; *Strongylus longevaginatus* Diesing, 1851, *Strongylus apri* (Gmelin, 1790) Blanchard, 1895; *Metastrongylus apri* (1790) Railliet and Henry, 1907

Biological and Geographical Data.—The worm is a common parasite of the lungs of pigs and wild boars, being present in the bronchioles and bronchi and at times in the trachea. Sheep and oxen have also been reported as hosts. It has been found three times in man, twice in the human respiratory tract [once by Diesing (1845) in a boy, aged six years, once by Rainey (1855) in an adult], and once in the digestive tract of a pork vender (Chatin, 1888).

This nematode is filiform in shape and creamy or brownish in color, and has a mouth bounded by a pair of lateral, trilobed lips, of which the median lobes are the largest. The buccal cavity is practically lacking. The esophagus is elongate and slightly club-shaped posteriorly. The males

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which the ventro-ventral and latero-ventrals are processes distinctly separated from one another, the externo-lateral is large and long and is clearly separated from the other laterals, the medio-lateral is broad and rounded, and the postero-lateral is represented by a small digitate process, the externo-dorsal is small and thin and the dorsal is a small bifurcated process The spicules are long (4 mm), hairlike structures, with a delicately hooked distal end (Fig. 240 *B*). The entire posterior end of the female is strongly recurved. The vulva is situated immediately in front of the anus (Fig. 240 *C*). The eggs are ellipsoidal, thick-shelled and vary in size from 57 to 100 μ by 39 to 72 μ. At the time of oviposition they contain well-developed rhabditoid larvæ According to Alicata (1934, 1935) they are usually evacuated as eggs in the mammalian host's feces, after being coughed up and swallowed. They may hatch soon thereafter on the soil to await ingestion by a suitable species of earthworm (as *Lumbricus terrestris*, *L. rubellus*, *L. rubida*, *Helodrilus fœtidus*, *H caliginosus*, etc.), in the esophageal or proventricular wall of which a required intermediate stage of development takes place In about ten days the larvæ grow from 0 22 to 0.35 mm in length to about 0 52 mm and pass through two ecdyses. The third-stage (infective) larvæ concentrate in the bloodvessels of the earthworm They do not spontaneously escape from this host but may be set free when the earthworm is injured or dies. Usually the infected lumbricids are eaten by the definitive host, thus transferring the infection.

Epidemiology.—In Nature pigs and earthworms alternate in carrying out the definitive and intermediate stages in the life cycle of this worm, with facultative periods of development or survival on the soil both before and after the stages of infection in the respective hosts. Man's infection is both accidental and incidental

Pathogenesis, Pathology and Symptomatology.—The lungs of infected pigs show whitish patches around the infected areas. In young pigs these worms

frequently give rise to a fulminating pneumonitis or bronchitis, which proves fatal.

Diagnosis.—On recovery of the characteristic eggs from the exudate of the respiratory tract or after having been swallowed and passed in the feces.

Therapeusis.—No specific chemotherapy is known.

Prognosis.—Fair in lightly infected animals; poor in heavily infected ones.

Control.—One of the human cases was a vender of pork. Infection in man undoubtedly occurs from contact with ground contaminated with the excreta of infected pigs. Feces of infected swine should be cleaned up regularly and kept off fields and runways. Uninfected swine should be kept separated from parasitized animals and should be removed to dry ground free of earthworms.

CHAPTER XXVII

THE PHASMID NEMATODE PARASITES OF MAN

(CONTINUED)

OXYURATA AND ASCARIDATA

Suborder Oxyurina (Cram, 1927) Pearse, 1936

(ENTEROBIUS AND RELATED FORMS)

THE members of this suborder are relatively small, unisexual, meromyarian species, of which the males have a reduced bursa or caudal alæ, supported by true but atypical rays, and one (exceptionally two) imperfectly chitinized copulatory spicules. The body of the females is drawn out into a point posteriorly. The eggs, which are oviposited in a fully embryonated state, are flattened on the ventral side. All of the known species are grouped under the type superfamily **Oxyuroidea** Railliet, 1916, which has the characteristics of the suborder. Six families of **Oxyuroidea** have been found in vertebrate hosts. The two oxyuroid species reported from man, *Enterobius vermicularis* and *Syphacia obvelata*, belong to the type family **Oxyuridæ**

Family OXYURIDÆ Cobbold, 1864

The species of this family have a posterior cardiac bulbus clearly separated from the anterior cylindrical part of the esophagus. The male worm lacks preanal suckers or other specialized muscles. The female is usually much longer than the male, and possesses a double germarium and connecting tubular oviducts and uteri, emptying into the vulva, which latter organ is usually preequatorial in position, but may be situated even as far posteriad as the preanal region. The eggs are ellipsoidal, fairly large and asymmetrical. No intermediate host is required for species of this family.

GENUS ENTEROBIUS LEACH, 1853

(genus from ἔντερον, intestine, and βίος, life)

Enterobius vermicularis (Linnæus, 1758) Leach, 1853. (The human pinworm or seatworm, causing human oxyuriasis or enterobiasis.)

Synonyms.—*Ascaris vermicularis* Linnæus, 1758, *Fusaria vermicularis* (Linnæus, 1758) Zeder, 1803; *Oxyuris vermicularis* (Linnæus, 1758) Lamarck, 1816, *Oxyuris vermicularis* (Linnæus, 1758) Bremser, 1819, *Oxyurias vermicularis* (Linnæus, 1758) Stiles, 1905; *Fusarella vermicularis* (Linnæus, 1758) Seurat, 1916.

Historical and Geographical Data.—The pinworm or seatworm of man has been known since ancient times. It is cosmopolitan in its distribution. Incidence of infection in a given population depends not so much on the climate or public sanitation as on the personal habits of the individuals in that population. In general, however, it is more prevalent among popula-

two specimens. Reardon (1938) has counted the eggs from 20 gravid specimens ranging in size from 6.7 by 0.3 mm. to 9.7 by 0.4 mm. and has

first-stage larva within (Fig. 241 *C*). In profile view they are flattened on one side (the ventral side) and are rounded on the dorsal aspect. They measure 50 to 60 μ by 20 to 30 μ. The transparent, partially refractive shell consists of two layers, an outer albuminous one, which tends to cause the eggs to agglomerate, and an inner embryonic membrane, probably of a lipoid nature. Preliminary to hatching the two membranes become separated except at one point on the dorsal surface just behind the cephalic pole.

Enterobius vermicularis requires neither an intermediate host nor any considerable period of incubation outside of the body. Eggs become infective within a few hours after deposition outside the anus and remain viable for several days. The intense itching, produced by the gravid females crawling out the anus and around in the perianal and perineal region, and by the deposition of the eggs, usually results in scratching of the affected area by the patient. This allows the eggs to get in under the finger nails, so that sooner or later some of them are taken into the mouth. Or, due to their ability to resist desiccation, they may remain attached to soiled bed linens and clothing or be transported by currents of air into the mouth or nares. In these ways they may be ingested or inhaled by the same or another individual and result in infection.

On reaching the duodenum the egg hatches and the rhabditoid larva is set free. This larva measures 140 to 150 μ in length by 10 μ in transverse diameter. It is only slightly active and is provided with no cephalic armature. *The development of the larva of Enterobius vermicularis* occurs without migration through the body of the host. After two moults in the small intestine, the adolescent worms mate and proceed to the large intestine, there to become attached to the mucosal layer and develop to adulthood. When the females become fully gravid, they release their hold on the intestinal wall and, on reaching the anus, pass out as previously described, and oviposit. The complete life cycle, as first worked out by Leuckart (1865), Grassi (1879) and Calandruccio (1888) and later by numerous other investigators, may be completed in as short a time as fifteen to twenty eight days (Cram, 1943).

Epidemiology.—Because no developmental stage is required outside the human body, this infection is more prevalent in individuals of the sam family or of an institutional group, such as a school, asylum or menta hospital, than it is in the population at large. It is more common in a mother and her small children than in the father and adult male children It is more common in large dormitory groups than in smaller ones. In homes where several children sleep in the same bed or even in the same room the incidence is higher than when each individual has a separate bedroom. It is more prevalent in the Caucasian than in the Negro race (Cram, 1941). In an infested house the eggs may be recovered in all of the rooms which are used but the largest number is found in the bedrooms.

Cool, moist surroundings with little or no ventilation are optimal for

survival of the eggs of *E. vermicularis*, while dry heat and good ventilation produce rapid desiccation of the eggs (Jacobs, 1941; Heller, 1944)

The incidence of oxyuriasis in children ranges from a relatively low figure to 100 per cent. Schüffner (1944) has reported the latter figure for Amsterdam, while Young (1942) gives 42 per cent as the rate for 119 children in St. Bartholemew's Hospital in London. Chanco and Soriano (1939) reported 75.2 per cent incidence in one swab examination of 431 school children and 59 adults in Manila Stoll, Chenoweth and Peck (1947) found only one per cent of 634 natives of Guam infected and none over fifteen years of age. Kuitunen-Ekbaum (1943) discovered 60 per cent infection in 300 non-institutionalized school children in Toronto. Cram (1943) reported 41.5 per cent positive among 2895 white school children and adults in Washington, D. C In South Dakota (U S.A.) 39.4 per cent of 315 children were found infected by three swab examinations. The incidence was appreciably higher in school children than in the pre-school group studied In Latin America the following percentages of infection have been reported· Puerto Rico, girls asylum, 30, boys asylum, 12 (NIH swab, Brady, 1941); Rio de Janeriro, 22.3 (finger nails, Corvalho, 1928); São Paulo (Brazil), 60 0 (cellophane swab, Cristovão, 1941); Buenos Aires, 42.0 (cotton swab, Bacigalupo, 1941), Mexico, D.F., 48.0–51.0 (cellophane swab, Osorio and Mazzotti, 1940, Mazzotti and Quintanar, 1943), and San José (Costa Rica), 4 3 (cellophane swab, Sutliff and Echandi, 1946).

The methods of transmission of oxyuriasis are four-fold. The foremost source is the anal and perianal region and the commonest means is direct anus-to-mouth by finger contamination Schuffner (1944) regards soiled night clothes as another anus-to-mouth transmission hazard in persons ... hanging to day- ... e viable eggs to ... an individual or group of persons who have similar habits. In the third place, airborne eggs, particularly those dislodged from bed linens and night clothes, which ...

large group of individuals in contact with the contaminated air. This is frequently the explanation for the high percentage of persons found infected by careful repeated swab examination. A fourth method has been demonstrated by Schuffner and Swellengrebel (1949), who have found in human volunteers under controlled conditions that in a moist environment infective-stage eggs at times hatch on the anal mucosa, and that the hatched larvæ migrate up into the bowel and develop into adult worms. These workers refers to this method as *retrofection*. As previously stated,

...

and inflammation of the intestinal wall to which the adult worms are attached; (2) *pruritus periani et perinei;* (3) neuroses resulting from (1) and/or (2) above, and (4), in the female patient, symptoms resulting from invasion of the female genitalia.

MacKeith and Watson, British pediatricians, have concluded that the most common symptoms of oxyuriasis consist of the triad (1) local itching, (2) restless sleep and (3) irritable tiredness.

Within the intestine the worms may occasion minute local areas of inflammation around the heads attached to the mucosal layer of the wall. The adult worms in the lumen of the appendix may mechanically or by lysis cause extensive hemorrhage or a catarrhal inflammation which may involve the *muscular layers or allow entrance of pathogenic bacteria. In a study of 330 appendices in Formosa, Ujiie (1935) found definite pathology* attributed to the pinworm (*appendicopathia oxyurica*) in sixteen of twenty in which *Enterobius vermicularis* was observed. *Necrosis of the mucosal* layer of the cecum may expose the sympathetic nerve endings and give rise to serious reflex symptoms. Migration out of the rectum frequently causes congestion of the anal region, with pin-point hemorrhages and erosion of the mucous membrane and, at times cutaneous eczema.

Around the anus, as well as within it, there may be developed an almost unbearable pruritus, which is temporarily relieved by scratching. Subcutaneous tumors of the anal region may also be produced. Irritation of the perineum may give rise to sexual perversion in both male and female subjects. *Occasionally the adult worms may wander into the upper levels* of the small intestine or be carried there by reversed peristalsis; they have *even been recorded from the stomach,* esophagus and nares.

In infants, and to a certain extent in adults, nervous symptoms of various types, due either to direct irritation or to specific toxins absorbed by the body, have been commonly observed. In females, a mild or a more profound hysteria may be produced; in children, loss of appetite, insomnia, extreme restlessness and incoordination and even epileptiform seizures may be occasioned by seatworm infection. Several cases are also on record in which the gravid female worms have migrated *through the vagina and* Fallopian tubules of female patients, where they have become encysted; or *they have wandered into the peritoneal cavity* and have become encysted in the peritoneum. In the tubules they may produce symptoms *simulating* salpingitis of gonococcus or *M. tuberculosis* origin (Wu, 1935).

In boys nycturia is not an uncommon associated symptom, which is relieved on eradication of the worms. There is at times ... may be a low grade a ... secondary anemia.

Diagnosis.—Oxyuriasis may be suspected from the clinical history but *specific diagnosis depends on recovery* of the egg or of the parent worm. The eggs of *Enterobius vermicularis* are found in the feces by direct smear examination in not over 5 per cent of infected persons. While a much better diagnostic showing can be made by bri[illegible] zinc sulfate *centrifugal* floatation technics (*vide* pp. 593 and 594), [illegible] consistently migrate out the anus to la[illegible] recovery of migrating worms or of eggs from the p[illegible] of choice.

For most satisfactory results the swabbing of the anal and perianal area should be made after midnight and before the morning bowel movement

and bath. Hellsten (1933) recommended wiping the outer part of the rectum with a vaselined cloth, shaking up the material obtained in a mixture of water and ether, centrifugalizing and then examining the sediment for eggs. The work of Hall and his colleagues (1937–1938) and of Sawitz, Odom and Lincicome (1939) has demonstrated the superiority of the cellophane anal swab (the NIH swab). (See Fig 243.) In 1942 Jacobs introduced a somewhat simpler swab technic, employing Scotch cellulose tape on the end of a wooden tongue blade, adhesive-side-out. At the time of swabbing the length of tape is held on the blade by the operator's index finger and thumb, and is then transferred, adhesive-side-down, to a microscopic slide for examination Mazzotti and Osorio (1945) rate the Jacobs technic as 50 per cent more efficient than the NIH swab. Schuffner and Swellengrebel (1943) have developed still another type of swabber, consisting of a 10 cm length thick-walled glass tube, with one end blown into a globe about 1 75 cm in diameter and ground rough This pestle end is dampened and then massaged over the perianal region. An emulsion of squamous cells, mucus, sweat and feces adheres to the swab It is claimed that the entire sample can be examined in 2½ minutes compared with 11 minutes for the NIH technic The pestle is easily cleaned by washing and can be used repeatedly. Petersen and Fahey (1945) recommend a clean glass slide with smooth ends for scraping the perianal skin. (For the preparation and use of these diagnostic aids *vide* pp 582–583) Adult worms, usually females, which have migrated on to the perianal skin, may be brought to the diagnostician as evidence of infection These must be distinguished from immature ascarids or other intestinal round-worms, as well as fly larvæ (maggots).

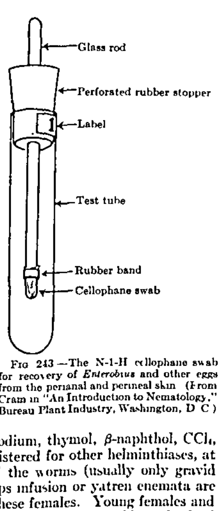


FIG 243 —The N-I-H cellophane swab for recovery of *Enterobius* and other eggs from the perianal and perineal skin (From Cram in "An Introduction to Nematology," Bureau Plant Industry, Washington, D C)

Therapeusis —Santonin, oil of chenopodium, thymol, β-naphthol, CCl_4, C_2Cl_4 and *Aspidium filix-mas*, as administered for other helminthiases, at times cause the elimination of some of the worms (usually only gravid females) High soap-saline, quassia chips infusion or yatren enemata are also frequently effective in evacuating these females. Young females and males attached to the mucosa of the large intestine are seldom obtained by any of these treatments

Wright, Brady and Bozicevich (1938) advocated *gentian violet medicinal* as a satisfactory anthelmintic in oxyuriasis. This has become the standard treatment for the infection. The drug is prescribed in Seal-Ins or Enseals

4-hour coated tablets, for adults two 0.03 Gm. (½ grain) tablets before meals three times daily for eight days, then rest one week and repeat treatment for another eight days. (Total drug for one course of treatment, 3.3 Gm. or 48 grains.) For children the recommended daily dosage is 1 *cgm.* for each year of apparent, not chronological, age. The tablets are available in the following sizes: 1 cgm. [illegible]

[illegible] producing cures, as determined by seven post-treatment swab examinations by the NIH technic. Petersen and Fahey (1945), who studied *gentian violet* therapy in 1100 (59 per cent) positives among 1871 patients in a mental hospital in Minnesota, administered the drug for three eight-day periods with eight days of rest between each two treatments. (Total drug: 4.6 Gm. or 72 grains.) Using a glass-slide scraper of the perianal skin, 9 per cent of the pre-treated positives remained positive following the first eight days of treatment; one per cent following the second period of treatment, and 0.2 per cent following the third period of treatment.

The week of rest between active periods of treatment is designed to allow time for viable eggs in the environment to gain entry to the intestine and hatch, so that the next period of treatment will kill larvæ derived from these eggs. If all positive cases in the group are treated simultaneously, all residual eggs in the environment beginning with the second eight days of treatment should be nonviable. In some patients various workers have reported considerable discomfort following administration of the anthelmintic, including nausea and vomiting, abdominal cramps, constipation, dizziness, headache and lassitude.

Kuitunen-Ekbaum (1946) has studied the efficacy and toxicity of *phenothiazine* in the treatment of oxyuriasis. The regimen of treatment was as follows for each of 4 days: for children under 2 years of age, 0.25 Gm. per diem, with a total dosage of 1 Gm.; 2–3 years, 0.5 Gm. daily, total 2 Gm.; 4–5 years, 0.75 Gm. daily, total 3 Gm.; 6–7 years, 1 Gm. daily, total 4 Gm.; 8–9 years, 1.25 Gm. daily, total 5 Gm.; 10–11 years, 1.50 Gm. daily, total 6 Gm.; 12 years and older, 1.75 Gm., total 7 Gm. Higher doses were too toxic, producing rapidly developing anemia, and had to be abandoned. Among 408 treated children, 80.2 per cent became negative after one course of treatment, 18.6 per cent additional after a second course and 1.2 per cent additional after a third course. Among 176 treated adults there was no significant difference in the percentage of negatives. Occasional fever, rash, pruritus and edema at times were associated with the treatment. Deschiens and Lamy (1947) regard phenothiazine as too toxic for routine administration. They reserve it for certain healthy adults but do not prescribe it for children under twelve years of age, or for adults with anemia, hepatitis or nephritis.

Pruritus ani, due to pinworms, should be treated by the application of mercurial or sulfa ointments. Invasion of worms into the appendix may produce appendicitis and require surgical intervention.

Prognosis.—Good, unless the infection gives rise to severe neuroses or secondary invaders gain entrance to the intestinal wall or to the general circulation through lesions produced by the worms.

Control.—Sanitary measures should be directed towards two ends, namely, prevention of (1) reinfection of an individual already harboring the worms, and (2) infection of contacts Pinworms are more common in children than in adults, they are usually more common in women than in men. This is due to contact between mothers or elder sisters and younger children. Familial infections are usual, one member of the family conveying the viable eggs to another. Infected individuals should be provided with protective sleeping garments so that their hands do not become contaminated during sleep All individuals should be taught to wash their hands thoroughly after visiting the toilet and before meals. Finger nails of infected persons should be cut short Toilet seats should be scrubbed with strong cresol solution two or three times a week, then rinsed with water and wiped dry. Nevertheless, all of these hygienic measures will probably prove futile unless all infected members of the family or institution are given adequate anthelmintic treatment. (*Vide supra.*)

Warm temperatures, a prevailing breeze, with a minimum of dust in the air, a minimum of clothing and frequent bathing are conducive to low incidence and light infections.

Genus Syphacia Seurat, 1916

(genus from σίφω, a tube)

Syphacia obvelata (Rudolphi, 1802) Seurat, 1916

Synonyms.—*Ascaris obvelata* Rudolphi, 1802, *Fusaria obvelata* (Rud , 1802) Zeder, 1803; *Oxyuris stroma* v Linstow, 1884, *Oxyuris obvelata* (Rud , 1802) Hall, 1916

This species of oxyurid nematode is characterized by having three broad lips

region is provided with a pair of relatively inconspicuous alæ Both sexes have a

5 1 6 mm in length by 0 1 mm in cross-
360 degrees ventrad There are two or
three cuticular mammillations on the ventral surface The pericloacal region is provided with a pair of pointed alæ There are two pairs of preanal papillæ and, in
addition, upport
the cauda The
short gub caudal
alæ is a stiff attenuated caudal extremity, measuring 0 12 mm in length
in cross-section
14C) The vulva
the cephalic end
ith a very muscu-
lar ovejector, which leads into a single, very long uterus This latter, in turn, is succeeded distally by a pair of narrow receptacula seminis, lying side by side Still farther distad are the two delicate oviducts and ovarian tubules The worms are
iculoris but are
They contain

The life cycle of this species is direct, without the intervention of an intermediate host. The infection is cosmopolitan as an intestinal parasite of rats and mice. One human case has been reported by Riley (1919) from an American child in the Philippines.

Human infection probably results from accidental contamination with droppings of infected murine hosts. As a result of apparent contamination by laboratory mice two specimens of children's stools and two of rhesus monkeys were diagnosed (1944) with typical *S. obvelata* eggs in the author's laboratory in Tulane University.

The clinical aspects of this infection have not been studied.

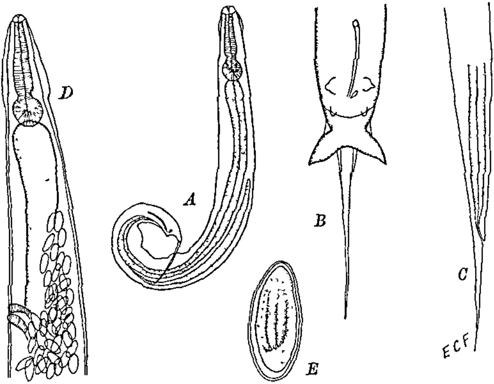


FIG. 244.—*Syphacia obvelata*. *A*, lateral view of male worm × 75. *B*, caudal extremity of male, ventral view × 330 *C*, posterior end of female worm, lateral view. × 215 *D*, anterior end of female worm, showing vulvar opening and uterus. × 330. *E*, egg, with developing larva × 150 (After Yorke and Maplestone.)

Suborder Ascaridina (Railliet and Henry, 1915) Pearse, 1936

(ASCARIS AND RELATED FORMS)

The members of [illegible] monomyarian or polymyarian species, in which there are [illegible] labia are lacking. [illegible] the other two are submedian and approximately ventral. The cep[illegible] papillæ consist of an inner circle of six and an outer circle of four well-developed double papillæ and two well-developed single papillæ. The excretory system is H-shaped. There is no buccal capsule. The males either have two copulatory spicules or a single spicule. The females commonly have two ovaries, but in species found in snakes there are more than two. The females are oviparous, the eggs being frequently unsegmented when oviposited. The development is usually direct, without an intermediate host, but a migration of the larvæ through the lungs of the host is

required in some species before the worms may develop to adulthood. At present all of the families of this suborder are placed in the superfamily **Ascaridoidea** Railliet and Henry, 1915, which has the characters of the suborder. All of the human representatives of the superfamily belong to the type family **Ascaridæ**.

Family ASCARIDIDÆ Baird, 1853

The mouth of members of this family is either provided with three prominent lips supplied with papillæ or with three primary lips and three secondary intermediate lips. The esophagus lacks a cardiac bulb. The males usually have two spicules. The tail of the female terminates conically and fairly abruptly. The vulva in most species is preequatorial in position. In the species reported from man the males lack a precloacal sucker.

GENUS ASCARIS LINNAEUS, 1758

(genus from ἀσκαρίς, helminth)

Ascaris lumbricoides Linnæus, 1758 (*The giant intestinal roundworm, causing ascariasis.*)

Synonyms.—*Stomachida teres* Pereboom, 1780, *Stomachida pereboomii* Goeze 1782, *Ascaris suum* Goeze 1782 (probably a physiological variety or subspecies), *Fusaria lumbricoides* (Linn., 1758) Zeder, 1800, *Lumbricoides vulgaris* Merat, 1821, *Ascaris suilla* Dujardin, 1845, (?) *Ascaris maritima* Leuckart, 1876, (?) *Ascaris texana* Smith and Goeth, 1904.

Historical Data.—*Ascaris lumbricoides* was well known to the physicians and naturalists of ancient times, since it was one of the most common helminths in all parts of the ancient world. The Greeks referred to it as ἕλμινς στρογγύλη; the Romans called it *Lumbricus*, the present-day name for the common earthworm. Although Kuchenmeister (1855) failed to produce infection by feeding embryonated eggs, Davaine (1863) discovered that they hatch in the small intestine. Stewart (1916) demonstrated that the hatched larvæ require a journey to the lungs, from which they return to the small bowel *via* the epiglottis, but since he was unable to rear these larvæ to adults in experimental mice and rats, he concluded that these animals served as intermediate hosts. However, Ransom and Foster (1917) and Ransom and Cram (1921) demonstrated that in the normal host, pig *Ascaris*, after migration to the lungs and return to the small bowel, developed into adult worms. It remained for the brothers Koino (1922) to prove the lung journey in human ascariasis by recovering the migrating larvæ in the sputum.

Ascaris lumbricoides of man and of the pig is morphologically indistinguishable. This same species has also been recorded for the monkey, the squirrel and more recently from the muskrat, *Ondatra zibethica* (Tiner and Chin, 1948). However, attempts at experimental infection have indicated that human and porcine *A. lumbricoides* are peculiarly adapted to their host and are highly refractory to reciprocal infection.

Geographical Distribution and Incidence.—Ascariasis is widely distributed throughout the world except in cold climates. In many extensive tropical regions with an annual rainfall of 100 centimeters or more practically every child is parasitized from early infancy, and the incidence figure for adults is 50 per cent or higher. Even in Temperate Zones, as in the southern part of the Appalachian highlands of the United States (viz., the western portion of Virginia, West Virginia, eastern Kentucky, eastern Tennessee and the

adjacent portions of the Carolinas, Georgia and Alabama) the percentage of infected persons, especially children, nearly approaches that of tropical countries, and the worm burden is heavy. The following percentages of infection have been reported for Europe: Copenhagen, 2.6 (Roth); Basel, 4.0 (Kreis); Zurich, 5.7 (Klotz and Sprizmann); Prague, 3.4 (Gabriel); Moravia, 4.0 (Kučera and Jirovec); E. Prussia, 52.0 (Vogel) and Carpathia, 51.7 (Dziuban). Stoll (1947) has estimated the world incidence of ascariasis to amount to 644.4 millions, consisting of 3.0 millions in North America, 42.0 in tropical America, 59.0 in Africa, 32.0 in Europe, 19.9 in the U.S.S.R., 488.0 in Asia and 0.5 in the Pacific islands.

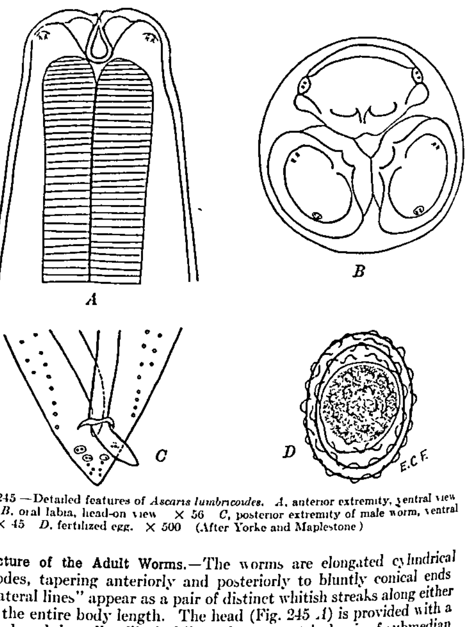


FIG. 245 —Detailed features of *Ascaris lumbricoides*. *A*, anterior extremity, ventral view × 46 *B*, oral labia, head-on view × 56 *C*, posterior extremity of male worm, ventral view × 45 *D*, fertilized egg. × 500 (After Yorke and Maplestone)

Structure of the Adult Worms.—The worms are elongated cylindrical nematodes, tapering anteriorly and posteriorly to bluntly conical ends The "lateral lines" appear as a pair of distinct whitish streaks along either side of the entire body length. The head (Fig. 245 *A*) is provided with a median dorsal, broadly elliptical lip and a symmetrical pair of submedian ventral oval lips, all of which are finely denticulate. Each lip has on each of its lateral margins a pair of minute papillæ (Fig. 245 *B*) There is a small buccal vestibule in the median axis beneath the lips and behind this a

cylindrical, muscular esophagus (10 to 15 mm. long), which lacks a ventriculus. As in other nematodes, the esophageal glands consist of a single dorsal member and two subventral members, each with a single nucleus The esophagus leads directly into the mid-intestine, which continues to the subcaudal extremity of the body, where it empties into a short rectum which opens directly through the anal pore in the female and into the cloaca in the male

The male worm has a length of 15 to 31 cm. and a transverse diameter of 2 to 4 mm Its posterior end is curved ventrad. The male genitalia form a long, tortuously coiled tubule situated in the posterior half of the body, consisting of testis, collecting tubules and ductus ejaculatorius, the latter opening into the cloaca. Dorsal to the posterior terminus of the ductus is the pocket into which the 2 equal, or subequal, unwinged, club-shaped spicules, of 2 to 3.5 mm. length, are retracted (Fig. 245 *C*). There is no gubernaculum. There are numerous preanal and postanal papillæ, situated symmetrically in four parallel lines preanally and in four groups of two and six single units postanally (Fig 245 *C*) In the recurved posterior portion of the male traces of caudal alæ are sometimes seen.

The female usually measures 20 to 35 cm in length by 3 to 6 mm. in transverse diameter. Occasionally specimens develop to a length of 40 to 49 cm. The vulva is situated near the junction of the anterior and middle thirds of the body. It leads into a conical vagina, which branches to form the paired genital tubules, each member containing uterus, receptaculum seminis, oviduct and ovary. These two members more or less parallel one another in a tortuous course throughout the posterior two-thirds of the body cavity. The uterine tubules are relatively broad and when stretched out may have a length of 200 mm. each The ovarian tubules with their ducts may each have a length of ca. 1250 mm. The total capacity of the ... is ... e,

The fertilized eggs (Fig 245 *D*, 246, 1) are broadly ovoidal in shape, with a thick transparent shell and an outer, coarsely mammillated, albuminous covering which is at times lacking and is not essential for embryonation. They measure 45 to 75 μ in length by 35 to 50 μ in lesser diameter. Eggs *in utero* are hyaline, but the albuminous layer becomes yellowish-brown from the bile pigment in the feces. At the time of oviposition the egg is

...

structure is unorganized and frequently contains large numbers of highly refractive granules. These eggs are most frequently passed by female worms when males are not present in the intestine of the host (6.37 per cent of cases), but appear with fertile eggs in 37 to 40 per cent of infections. In 3.34 per cent of 1820 children examined by Yokogawa and Wakeshima (1932) only male worms were present

Development of the Eggs and Larvæ.—The development of *Ascaris lumbricoides* eggs is directly influenced by temperature, moisture and oxygen

supply. In night-soil mixtures or in a cold, dry climate they remain practically dormant. Yet freezing and desiccation not only do not ordinarily kill the eggs, due to the extremely good insulation afforded by the shell layers, but, on the other hand, frequently stimulate development. Temporary baths in strong chemicals, such as glass-cleaning solution, are not injurious

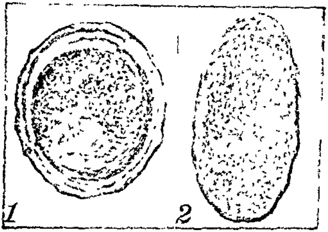


FIG. 246.—Photomicrograph of eggs of *Ascaris lumbricoides*. 1, Fertilized, 2, unfertilized egg. × 600. (After Faust, in Brennemann's Practice of Pediatrics, courtesy of W. F. Prior Company.)

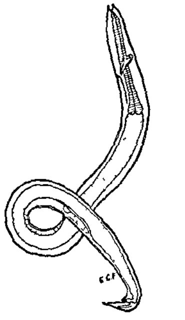


FIG. 247.—Larva of *Ascaris lumbricoides* from trachea of experimentally infected rat eight hours after ingestion of embryonated eggs. × 320. (After Brumpt, Précis de Parasitologie.)

to the embryo and moderately strong solutions of formaldehyde accelerate development of the embryo *in ovo*. At 22° to 33° C. the embryo develops in nine to thirteen days or more into a coiled rhabditoid larva. Eggs in contaminated soil may apparently remain viable for five or six years. At 45 to 50° C. the eggs are killed in 30 minutes; at 55° C., in 15 minutes; at 60 to 65° C., in 5 minutes, and at 100° C., almost instantly (Unat, 1942).

The infective-stage eggs each contain a motile rhabditoid larva. This is the second-stage larva, which develops from the first-stage larva about one week after the latter has become motile (Ransom and Foster, 1920; Ransom, 1922; Roberts, 1934; Alicata,

ing but soon succumb to the direct rays of the sun. While these eggs occasionally hatch in soil due to contact with water after a period of desiccation (Brown, 1928) or after abrasion with sand (McRae, 1935), there is no convincing evidence that infection normally occurs *via* the skin route.

Infection.—No intermediate host is utilized by *Ascaris*. The normal mode of infection consists in the ingestion of the mature, viable eggs con-

hours later through a V-shaped slit in the shell. The sheath (of the first-stage larva) is shed just before hatching. The larvæ which emerge from the shell are elongate, cylindrical objects, tapering at both ends, and measuring 0.2 to 0.3 mm. in length by 13 to 15 μ in transverse diameter. They are typical rhabditoid larvæ (Fig. 247), with a cylindrical esophagus, measuring 78 to 90 μ in length and enlarged posteriorly into a cardiac chamber, and with an elongate intestine and a short rectal-cloacal portion

Route of Migration Through the Body of the Host.—Stewart (1916) first showed that an extra-intestinal migration of *Ascaris* larvæ is normally required before they can proceed to complete development in the intestine. Ransom and Foster (1917) and Ransom and Cram (1921) demonstrated that the larvæ penetrate through the intestinal wall into the lymphatics and mesenteric veins, are carried to the right heart, either by way of the

' thence to the lungs. Here they
few days perforate the walls of
period of growth and two addi-
tional ecdyses (the first after five or six days, the second after the tenth day), migrate to the small intestine by way of the bronchi, trachea, epiglottis, esophagus and stomach During this period some larvæ occasionally migrate into aberrant foci, such as the peripheral lymph nodes, the thyroid, thymus and spleen, and even the brain and spinal cord, and in so doing may give rise to unusual symptoms Following heavy inoculation the larvæ may even be excreted in the urine. The period of migration is one of growth for the larvæ, they commonly increase in length during this passage from 0 2 or 0.3 mm. to 1.0 or 2.1 mm (average, 1 5 mm).

After arrival in the intestine of man, on the fifth day after inoculation or later, the larvæ of *Ascaris lumbricoides* originating from a human source develop to adulthood, likewise those in the pig originating from porcine ascarids complete their development. But porcine *Ascaris* larvæ in man and human *Ascaris* larvæ in the pig are apparently unable to complete their development in the reciprocal host In guinea-pigs, rats and mice, *Ascaris* larvæ from either human or porcine sources, on reaching the intestine after migration through the lungs, are rapidly eliminated. A fourth (and final) ecdysis occurs in the intestine between the twenty-fifth and the twenty-ninth day This is required before the worms can mature into adults In the appropriate host the worms reach full maturity two to two and a half months after exposure to infection, and the females begin to lay eggs.

Epidemiology.—Although ascariasis is practically cosmopolitan in its distribution, it is much more prevalent in the warmer than in the colder zones. It is a major parasite entity in tropical populations, particularly in children, and is an important helminthiasis in certain groups in temperate countries. Compared with the hookworm, *Ascaris*, as a soil polluter, is able to withsta
not surviv
viable on ......

survive well only in sandy humus. Ascariasis is an infection of all ages, but in most countries children under ten years of age are both more commonly and more heavily parasitized. They "seed" the soil with the eggs by promiscuous defecation, especially around dooryards. The infective-stage eggs are, in turn, most commonly picked up by young children from the ground which they or their playmates have previously polluted (Cort, 1931; Otto, 1932; Headlee, 1936).

FIG. 248.—Lung of experimentally infected mammal, showing larvæ of *Ascaris lumbricoides* in alveoli and white-cell infiltration around parasitized air spaces × 100. (Original photomicrograph.)

Pathogenesis, Pathology and Symptomatology.—The lesions produced by the worms and the symptoms occasioned by their presence in the human body may be divided into two periods, (1) the stage of migration and (2) the adult stage of the worm.

1. *The Stage of Migration.*—The minute lesions and petechial hemorrhages produced by the newly-hatched larvæ penetrating through the intestinal wall into the lymphatics and mesenteric veins, or later *en route* through the liver, are rarely sufficient to produce clinical symptoms. Upon arrival in the lungs the larvæ break out of the capillaries and set up inflammatory processes (Fig. 248). In mild infections there are numerous

petechial hemorrhages at the points of emergence into the alveoli In more heavily infected cases the entire lungs may be ecchymotic and edematous Microscopically there are many small inflammatory foci throughout the organ, with a marked exudate into the respiratory passages, consisting of red blood cells, leukocytes, desquamated epithelium, fibrin and migrating larvæ. Local eosinophilia is very marked The picture is that of multiple lobular pneumonitis. In extreme cases the lungs may be extensively involved, are edematous, hemorrhagic and completely consolidated

During the early part of the migration period the larvæ are believed to feed only on blood plasma, but later they have been found to utilize erythrocytes as food (Smirnov, 1935).

Clinically, the migration period is frequently accompanied by a chilly sensation or even a true chill, fever (38.5 to 40° C.), and eosinophilia may be demonstrated. At times there is bronchial irritation, with coarse and

or seventh day after exposure, small children, in whom there is a massive migration of the larvæ, may succumb to a fulminating, atypical pneumonia. In patients constantly exposed to infection, a chronic pulmonary syndrome may be found (Leitch, 1929; Girges, 1934)

Fisk (1939), likewise, reported a series of 120 autopsies of natives of Lagos, Nigeria, in which helminths of the intestinal tract (*Ascaris*, whipworms and hookworms) were found in large numbers Bronchopneumonia was *the most common* cause *of death* in children of ten years or younger (50 per cent). In this age group *Ascaris* was almost consistently present from five months after birth and conceivably could have been the etiological agent of the pneumonia.

In addition to the lesions produced by *Ascaris* larvæ in the lungs, there are transient microscopic changes in the liver, including small inflammatory foci throughout the organ, but not *involving the liver cells* *Larvæ that* get into the general circulation may reach the kidneys, brain, spinal cord and muscles of th … serious lesions Several investigat … ichi (1925) and Fulleborn (1929) … brain of experimental animals exposed to human *Ascaris* infection. Usually the larvæ, at times almost adolescent worms, remain in the cerebral arterioles which they block, but at times after penetration into the brain substance, with occasional granulomas. However, the most frequent finding consisted of hemorrhages, in the meninges but particularly in the cerebellum and floor of the fourth ventricle. Rarely *Ascaris* larvæ reach the ophthalmic artery and, lodging in the small vessels in and around the eyeball, produce retinal, choroidal or intracorneal hemorrhages, or they may escape into the vitreous (Calhoun). Acute nephritis has been observed in heavy infections, with larvæ in the urine.

2. *The Adult Stage of the Worm.*—The maturing and adult worms normally live in the lumen of the small intestine, feeding on the semidigested food mass, and at times on small bits of intestinal mucosa which

they may obtain by temporary attachment to the villi. It is even possible that they may occasionally suck blood from the bowel wall (Brown, 1934).

The number of ascarids present in the human bowel will vary from a single female, or rarely a single male, to many hundreds. It is not unusual to find several hundreds in children under five years of age in the Pediatric Service of the Charity Hospital in New Orleans. Where large numbers are present, there is characteristically considerable variation in their size and stage of maturity, from mature individuals somewhat smaller than average to those which have recently arrived from the lungs and are no larger than a small pin. According to Fülleborn (1932) Ryrie found 1488 worms in one case which came to autopsy. In infections consisting of only a few worms patients may suffer no appreciable inconvenience, but even a single worm may produce digestive disturbances. *The most common complaint is intermittent intestinal colic.* In children with *Ascaris* infection there is characteristically a protuberant abdomen. Normal digestion is disturbed; there is loss of appetite and insomnia. Small children are peevish and frequently cry out in their sleep. Infected individuals sensitive to *Ascaris* emanations may develop generalized toxemia or specific nervous complications. Reflex nervous symptoms are particularly common among small children.

Surgical Complications in Ascariasis.—Due to the relatively common occurrence of intestinal ascariasis and to the prevalent idea of its harmlessness, the seriousness of many cases is frequently overlooked. Milwidsky (1945) has outlined the types of complications in which immediate surgical intervention is demanded. (1) There may be a sudden development of *ileus*, which may result from mechanical obstruction from a twisted mass of writhing worms; it may be paralytic, spastic, invaginative or volvular in nature. (2) *Perforation* of the bowel may occur, particularly in the region of the ileo-cecal valve (See Fig. 249). (3) Not infrequently there may be an acute *appendicitis* or a *diverticulitis* (Milwidsky, 1945). (4) *Gastric or duodenal trauma* may result, suggesting peptic ulcer. (5) There may be *blockage* of the ampulla of Vater, of the common bile duct or entry into the parenchyma of the liver. Yang and Laube (1946) refer to 90 cases of biliary ascariasis collected by Aviles (1918), 12 more discovered at autopsy in the Philippines, 9 cases reported by Morton (1928), 30 additional cases of Ch'in (1933, 1937), 3 of Ch'en (1943) and 18 more observed in Chengtu, West China during 1943–1946. These patients complained of radiating epigastric or right quadrant pain, vomiting and other symptoms suggesting cholelithiasis. Additional cases not known to Yang and Laube (l.c.) have been published (Li, 1945; Malice, 1945, etc.). (6) Chin (1933) reported one case of acute *hemorrhagic pancreatitis*. (7) *Ascaris* has been found as the probable etiologic agent in *pleural empyema* and *pulmonary gangrene* (Stiles, 1921; Middleton, 1929). (8) Rarely this worm may cause sudden *obstruction of the larynx* (Dixey, 1929) or (9) *esophageal perforation*. (10) There are numerous records of *genito-urinary tract involvement*, including obstruction of a Fallopian tubule (Maxwell, 1924; Sterling, 1936), and blockage of the bladder or urethra (Carsten, 1927; Liu and Wang, 1941). (11) There is a single, almost increditable finding of *invasion of the heart* by an *Ascaris* (Boettiger and Werne, 1929). *Ascaris* may be passed

spontaneously *per anum*, may wander into the stomach and be vomited, or may escape through the nares.

In addition, ascariasis may produce symptoms of meningitis or of epilepsy, or there may be ocular disturbances, especially hemorrhage into the retina or vitreous, with associated palpebral edema (Drouet, Thomas,

FIG. 249.—*Ascaris lumbricoides* blocking the appendix of a child, aged six years, with *antemortem* diagnosis of "acute abdomen." Exploratory celiotomy revealed 9 worms in the peritoneal cavity in addition to others which were blocking the appendiceal lumen. The child died of peritonitis. (Original photograph, courtesy of Dr. Samuel Field and Dr. Robert Strong.)

Herbeuval and Faivre (1945). Occasionally there may be hematuria (Mathieu and Faivre, 1935) or hemorrhagic nephritis (Drouet *et al.*, l.c.). Finally, the presence of *Ascaris* may be responsible for a misplaced diagnosis of abdominal tumor or of gastric or duodenal ulcer.

The blood picture is not pathognomonic, although there may be a low-grade anemia and an eosinophilia of 7 to 12 per cent or more may be present.

Diagnosis.—*Clinically* the presence of *Ascaris* in the body is accompanied by symptoms which range from essentially asymptomatic to very grave. The manifestations are protean and there is no distinct syndrome. In bronchopneumonia, ac acute pancreatitis and many as loss of appetite and weight, insomnia, nervous states, and even ocular disturbances, ascariasis must be considered. A history of residence in an endemic area, particularly in the case of small children, adds considerable weight to claims for consideration. The spontaneous passage of adult or immature ascarids *per anum, per os* or *per narem* provides specific evidence that infection has occurred and may still exist.

The presence of adult ascarids in the bowel can be diagnosed on the basis of finding the fertilized or unfertilized eggs in the stool, except in infections where only male worms are present, a condition not unique in children. Under the latter circumstances diagnosis must be made clinically and checked by the therapeutic test. A diagnosis of *Ascaris pneumonia*, corresponding to the period of larval migration through the lungs, can be made only tentatively, to be checked by examination of the feces some weeks later when the worms become egg-laying adults in the intestine.

Therapeusis.—Treatment of *Ascaris*-infected patients in former years was primarily dependent on the administration of santonin or oil of chenopodium. The efficiency of santonin is very much lower than that of oil of chenopodium, but because of its relative safety, it has been the drug of choice, particularly for administration to children.

Santonin does not irritate mucous membranes and is essentially non-toxic to the respiratory and circulatory systems, although it injures the central nervous system and the centers of the special senses, which it tends to paralyze (Desoille, 1937). As an anthelmintic it rarely kills *Ascaris* and in therapeutic doses has a worm-removal rate of about 27 per cent (Hall and Augustine, 1929). A tolerated dose (0.06 to 0.2 Gm.) is combined with calomel (0.2 to 0.3 Gm.) and should be followed by saline purgation. It should never be administered on an empty stomach.

Oil of chenopodium, or its effective fraction (*ascaridol*), is too toxic for recommended use in full therapeutic amounts (3 to 4 cc.). However, in cases of hookworm infection accompanied by ascariasis, tetrachlorethylene or carbon tetrachloride in the amount not in excess of 2.7 cc. with 0.3 cc oil of chenopodium for an adult, 3 minims of the combined drugs for each

ascarids. It does not remove the worms but frequently stimulates them to excessive movement, which is harmful, and occasionally fatal, to the patient. *Tetrachlorethylene* has practically no value in ascariasis. *Gentian violet medicinal* has only slight anthelmintic properties against *Ascaris*, although its administration for strongyloidiasis or oxyuriasis is not contra-indicated by the presence of *Ascaris* (Brown, 1946).

Crystoids anthelmintic (hexylresorcinol crystoids) is the drug of choice in

treating ascariasis; it is both highly efficient and essentially non-toxic in *Ascaris*-infected patients. The drug is available in hard gelatin capsules, in 0.1 and 0.2 Gm. sizes. This anthelmintic acts by penetration of the worm's cuticula, which is increased greatly in the presence of very low concentrations (0.05 per cent) of sodium oleate (Trim, 1944). In therapeutic doses, taken on an empty stomach, the drug has an *Ascaris*-removal rate of 84 to 92 per cent and a cure rate of 75 to 80 per cent (Lamson, Brown, Robbins and Ward, 1931). For an adult or a child over ten years of age, 1.0 Gm. is the indicated dose, for children of pre-school age, 0.4 to 0.6 Gm.; for children in elementary schools, 0.6 to 0.8 Gm. The medication is given in the morning on a fasting stomach, with care not to crush the capsules before swallowing. A normal noon meal may be taken. While purgation is not necessary to prevent toxic symptoms from the drug, it is desirable to evacuate dead or dying worms. If hypermotility of the bowel is demonstrated, greater efficiency will probably be obtained by omitting the post-treatment purge.

Surgical interference is indicated where acute obstruction has been produced. In these cases purgation and anthelmintic medication are absolutely contraindicated.

It is important to remember that ascaricidal drugs are effective only after the worms have completed their lung journey and have become resident in the small bowel. There is no known anthelmintic treatment for the larval worms in migration.

Prognosis.—*Ascaris* infection is not serious except in profound *Ascaris pneumonia*, acute intestinal or biliary-duct obstruction or perforation of the intestine.

Control.—Ascariasis is common in all tropical and Oriental countries and

of considerably greater exposure. The investigations of Cort and his colleagues (1928–1933), of Headlee (1936) and of other epidemiologists have demonstrated that ascariasis is primarily a dooryard infection, and that children "seed" the soil with the eggs of this parasite, because there are

n.

s alone is

"*Ascaris*

environments" and soon pick up new infections, which may have been deposited on the soil many months previously (Headlee, 1936). Thus, in every *Ascaris* family or community intensive hygienic measures are needed. Every home should have a sanitary toilet (or in tropical countries, adequate sanitary group latrines), and small children must be taught to use them consistently (Cort, 1931). Such instruction can most effectively be carried out in the elementary schools, and through them to the homes.

In addition to direct exposure from "infective soil," in areas where human nightsoil is used as fertilizer for truck crops, as in the Orient, infection is not uncommonly acquired from the consumption of raw roots, stems, leaves and fruits which develop in, on or near the ground (Walker, 1927, in

nd Sumi,
S. S. R.)
sources of infection, fully embryonated *Ascaris* eggs are at times taken off the ground and carried by air currents, and in this way may get into the throat and be swallowed. Bogojawlenski and Demidowa (1928) found *Ascaris* eggs in the nasal mucus of 3.2 per cent of school children whom they examined R. Cram and Hicks
, present in sludge in a
content is reduced to 5 per cent or less or if the temperature is raised to 50° C. or above. Methyl bromide treatment kills only unembryonated eggs.

While there is the remote possibility that man may occasionally become infected with *Ascaris* from swine, by and large, man is the source of his own *Ascaris* infection, and preventive measures should be directed towards this end.

Genus Toxocara Stiles, 1905

(genus from τόξον, bow, and κάρα, head)

Toxocara canis (Werner, 1782) Johnston, 1916. (The dog ascarid.)

Synonyms.—*Lumbricus canis* Werner, 1782; *Ascaris canis* (Werner, 1782); Gmelin, 1790; *Ascaris mystax canis* (Werner, 1782) Blanchard, 1888, Railliet, 1893; *Toxascaris limbata* Railliet and Henry, 1901; *Toxascaris marginata* Leiper, 1907; *Toxascaris canis* (Werner, 1782) Castellani and Chalmers, 1913; *Belascaris canis* (Werner, 1782) Garin, 1913.

co.
The males are 4 to 6 cm. long and the females 6.5 to 10 cm. long. The worm (Fig.
oped oral structure of the
extend some distance from
are much longer than broad, and in cross-section (Fig. 250*B*) have a deeply cleft, three-pronged core, which supports almost the entire wing structure. At the posterior end of the male (Fig. 250*C*) there is a series of several pairs of pedunculated, and three pairs of sessile papillæ. The spicules are long and curved, slightly unequal, and in cross-section (Fig. 250*D*) are appreciably convexo-concave. The vulva of the female is situated
The eggs (Fig. 250*E*)
and measure 85 to 75 μ

According to Wright (1936) there are four larval stages

The adult dog is practically unaffected by the presence of this worm in its intestine. It is congenitally transmitted by mother dogs to their young, which frequently succumb to the infection during the first two or three weeks of life. According to Brumpt, three or four months after maturing, the worms are eliminated spontaneously from the host, which becomes immune to reinfection.

Toxocara cati (Schrank, 1788) Brumpt, 1927. (The cat ascarid.)

Synonyms.—*Ascaris cati* Schrank, 1788; *Fusaria mystax* Zeder, 1800; *Ascaris mystax* (Zeder, 1800) Rudolphi, 1802, *Ascaris alata* Bellingham, 1839; *Ascaris felis* Glaue, 1909; *Belascaris mystax* (Zeder, 1800) Castellani and Chalmers, 1910; *Belascaris cati* (Schrank, 1788) Railliet and Henry, 1911.

This is the common ascarid in the intestine of the cat, in which host it is cosmopolitan It has also been recorded from the wild cat, the lion, the leopard, *Felis minuta* and *F. maniculata*. There are 10 recorded cases of this infection from the human host in Europe and North America (Swartzwelder, 1941), but the possibility of spurious parasitism in some of these reports is not excluded An example is the case brought to the author's attention, in which it was found that a child, in whose stool eggs of *T. cati* were once diagnosed but whose later stools were negative, had innocently swallowed feces of a pet kitten The adult worms (Fig 251*A*) are

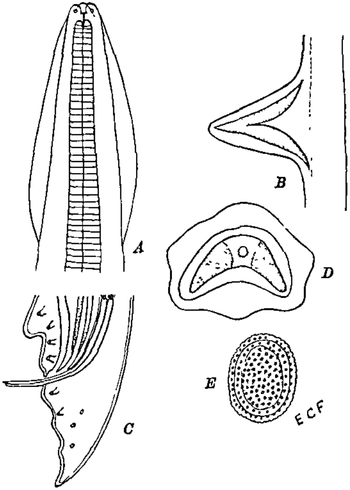


FIG. 250 — *Toxocara canis* *A*, anterior end of worm, ventral view, showing labia and cervical alæ, × 30, *B*, detail of cross-section through cervical region, showing structure of ala; *C*, posterior end of male, lateral view, showing cloaca, with adjacent portions of rectum, ductus ejaculatorius, copulatory spicules and preanal and postanal papillæ, × 50, *D*, cross-section through spicule, with enveloping sheath, *E*, egg × 250 (Original)

characterized by having, on the border of the cervical region, a heart-shaped lateral

graphic arrangement is somewhat different. The copulatory spicules
measure 1.7 to 1.9 mm. in length
bequal,
to have

uterine duct is long.
pitted, and measure (
and other unfavorabl
environment.

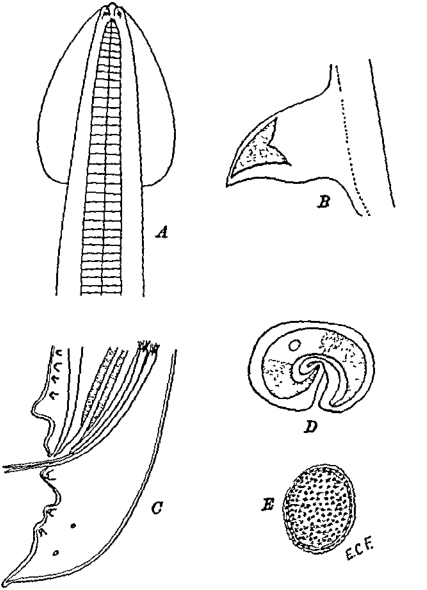


FIG 251 —*Toxocara cati*. A, anterior end of worm, ventral view, showing labia and cervical alæ, × 30; B, detail of cross-section through cervical region, showing structure of ala; C, posterior end of male, lateral view, showing cloaca, with adjacent portions of rectum, ductus ejaculatorius, copulatory spicules and preanal and postanal papillæ, × 50; D, cross-section through spicule with enveloping sheath, E, egg, × 250. (Original)

the part of their hosts.

Genus Lagochilascaris Leiper, 1909

(genus from λαγώς, and χεῖλος, hare-lipped, and ἀσχαρίς, helminth)

Lagochilascaris minor Leiper, 1909

Synonym.—*Lagocheilascaris minor* Leiper, 1909 of Fantham, Stephens and Theobald, 1916

The normal habitat of this worm is the intestine of the cloudy leopard, *Felis nebulosa.* Specimens of this species, sexually mature, have been found in man 5 times, from subcutaneous abscesses in the neck, in the vicinity of the angle of the jaw, in the orbit, and in tonsillar abscess pockets in 4 natives of Trinidad; and also from a mastoid abscess of a patient in Dutch Guiana. The male worms measure 9 mm in length by 0.4 mm. in transverse diameter and the females, 15 mm. in length by 0.5 mm in thickness. The parasites lack cervical alæ but have a triangular keel-like cuticular ledge along practically the entire extent of each lateral line. The three large lips are covered by a heavy investment of cuticle, each one having a distinct vertical cleft, the entire labial structure being separated from the body by a

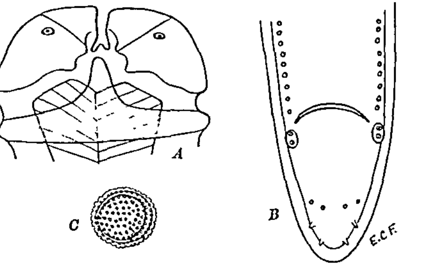


Fig. 252.—*Lagochilascaris minor* *A*, anterior end, showing the two ventral lips and the intervening ventral groove, *B*, posterior end of male, ventral view, showing cloacal opening and adjacent papillar pattern *C*, egg, × 250 (After Leiper, Proc Zoöl. Soc London)

deep annular furrow (Fig 252*A*) The male has about 24 pairs of preanal papillæ and 1 double pair and 4 single pairs of postanal papillæ (Fig. 252*B*) The copulatory spicules are solid colorless rods measuring 0.35 mm. and 0.4 mm. respectively in length The vulva is prequatorial in position The unbranched portion of the uterine tube is directed anteriad from its vulvar opening The ovaries and uteri lie in the middle third of the body The eggs (Fig 252*C*) are globose, clear in color, thick-shelled, and have superficial pittings like those of *Toxocara cati.* They measure 65 μ in diameter

Nothing is known about the life cycle of this nematode, but infection is probably direct, the worms in the human host becoming lodged in abnormal foci during their migration route through the body, and developing there into mature specimens.

CHAPTER XXVIII

PHASMID NEMATODE PARASITES OF MAN (CONTINUED)

SPIRUROID FORMS

Suborder Spirurina (Railliet and Henry, 1915) *Pearse, 1936*

(Synonyms, Spirurata Railliet and Henry, 1915, Filariata *Skrjabin*, 1915; Filarida Sprehn, 1927)

THIS suborder contains an assemblage of species of diversified types, but having the common characteristics of being long and usually attenuate, with a slender esophagus lacking a cardiac bulb. The females are larger than the males. The life cycle involves one or more intermediate hosts, of which the first is probably in all cases some species of Arthropod. Human representatives are found in the superfamilies **Spiruroidea** Railliet and Henry, 1915, and **Filarioidea** Weinland, 1858.

SUPERFAMILY SPIRUROIDEA RAILLIET AND HENRY, 1915 (SPIRUROID FORMS)

This superfamily comprises those species of filiform or somewhat more robust type, with or without pseudo-labia, having a slender esophagus; an intestine without diverticula; caudal alæ commonly present in the male; copulatory spicules usually unequal; and a vulvar opening frequently equatorial in position. The species parasitic in man are grouped in the families **Spiruridæ** Oerley, 1885, **Gnathostomatidæ** Blanchard, 1895, **Physalopteridæ** Leiper, 1908, **Thelaziidæ** Railliet, 1916 and **Acuariidæ** Seurat, 1913.

Type Family SPIRURIDÆ Oerley, 1885

The members of this family possess two or four trilobed, lateral pseudolips, and at times accessory ventral labia. There is a chitinoid oral vestibule in front of the esophagus. In the male the well-developed caudal alæ are supported by pedunculated papillæ. The females are oviparous (or ovoviviparous). The adults are parasitic in the tissues of the digestive tract of vertebrates. The eggs contain mature larvæ at the time of oviposition. The worms require an intermediate insect host, in the tissues of which the larvæ become encysted. Cases of human infection with spirurid nematodes have all been diagnosed as belonging to the genus *Gongylonema*. These worms should probably all be designated as *Gongylonema pulchrum*. In addition, there is the rather remote possibility of human infection with species of *Habronema*. (*Vide infra.*)

GENUS GONGYLONEMA MOLIN, 1857

(genus from γογγύλος, round, and νῆμα, thread)

Gongylonema pulchrum Molin, 1857. (The gullet worm, producing gongylonemiasis.)

Synonyms.—*Filaria labialis* Pane, 1864, (?) *Filaria scutata* Leuckart, 1873; (?) *Spiroptera scutata* (Leuckart, 1873) Korzil, 1877; (?) *Gongylonema scutatum* (Leuckart

1850, *Gongylonema* ...

(?) *Gongylonema ransomi* Chapin, 1922.

Historical and Geographical Data.—This parasite was first reported from man by Pane in Italy (1864). At least ten additional human infections have been placed on record: 1 from Italy by Alessandrini (1914), 6 from the United States (1 by Ward, 1916, from the lower lip of a sixteen-year-old white girl in Arkansas, 1 by Stiles, 1917, from the lip of a white woman in Florida; another by Stiles, 1921, from ... by Stiles and ... Virginia and a ... which a worm ... the lingual gum behind the front teeth of a patient;" 1 by Ransom, 1923, from the buccal mucosa of a young white male in Louisiana, and 1 by Waite and Gorrie, 1935, from the hard palate of a thirty-year-old white male in Alabama), 1 from Kharkov, in the Ukraine, U S S R ... Jugoslav, ...

Status ... nematodes secured from various definitive hosts is very unsatisfactory, due to disagreement of various investigators as to what characters may be relied upon for species differentiation in this genus Thus, there may be one to six different species in the group placed with son ... *Gongylonema pulchrum*, while ... *spirale* Molin, 1857 and even *G* ... synonymous with *G. pulchrum* ... size variation of the worms, in the different definitive hosts, in the range of size of ...

(*G r*...

The ...

Structure and Life Cycle ... which the parasite develops to a maximum size, as the optimum hosts and the pig and man as somewhat less suitable for its complete development. The male reaches a maximum length of 62 mm. by 0.15 to 0.3 mm. in diameter, and the female, 145 mm by 0.2 to 0.5 mm. The anterior extremity (Fig 253 *A*, *B*) is ... usually arranged in ... four submedian fields. ... side, is found about 0.1 to 0.2 mm. from the anterior extremity. Slightly behind these there arises a pair of cervical alæ, which terminate a short distance in front of the posteriormost cuticular bosses. The entire cuticle is characterized by the possession of fine transverse striations. The mouth is small and is provided with a funnel-shaped cuticular rim, immediately behind which there is believed to be a group of six minute cephalic papillæ.

The buccal vestibule consists of a short capillary tubule, varying from 40 to 80 μ in length. The anterior portion of the esophagus is a cylindrical muscular tube; the posterior portion is longer and stouter, and has glandular walls. The excretory pore is situated in a small crater-like projection of the cuticula on the ventral side, a short distance in front of the junction of the two portions of the esophagus.

The caudal end of the male (Fig. 253 *C*) is provided with distinct lateral alæ, which are appreciably asymmetrical, the member on the left side arising further anteriad and also extending around the caudal tip. There are from 2 to 8 (usually 5) pairs of subventral, pedunculated preanal

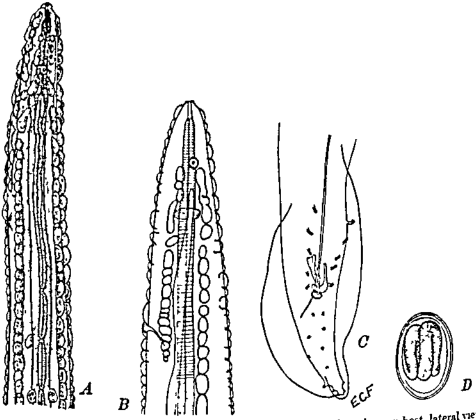


FIG. 253.—*Gongylonema pulchrum*. *A*, anterior end of worm from human host, lateral view, × 76 (after Ward, in Journal of Parasitology); *B*, anterior end of worm from reservoir host, lateral view, × 80 (after Baylis), *C*, posterior end of male, ventral view, showing alæ, caudal papillæ, spicules and gubernaculum, × 80 (after Baylis), *D*, egg, with coiled larva, × 375 (after Fibiger.)

papillæ, 4 pairs of subventral, pedunculated postanal papillæ and usually 4 pairs of minute papillæ at the caudal extremity. The two copulatory spicules are extremely unequal in length and dissimilar in appearance The left spicule is long (4 to 23 mm.) and narrow, with a tubular shaft and narrow membraneous alæ. The right spicule is short (not over 0.18 mm) and broadly winged. The gubernaculum has a V-shaped anterior portion and an expanded posterior part.

The posterior end of the female is asymmetrical, bluntly conical. The vulva is thick-walled and is slightly protuberant, being situated some little distance in front of the anus, which is subterminal. The vagina is very

long, extending anteriad from the vulva to the equatorial region. The divergent uteri extend nearly to the extremities of the worm, where they

the capillary ovaries.

D) are embryonated

...y 25 to 37 μ in lesser diameter.

When evacuated in the feces of the host, the eggs remain dormant until swallowed by an appropriate insect, whereupon they hatch in the digestive tract of this insect The emerging larvæ perforate through the intestinal wall into the hemal cavity and become encapsulated. They normally reach the definitive host again by being ingested along with the insect host. Ransom and Hall (1915) showed experimentally that several species of dung beetles of the genera *Aphodius* and *Onthophagus* as well as the small cockroach, *Blattella germanica*, serve as intermediate hosts of the form *G scutatum*, while Baylis, Sheather and Andrews (1925) demonstrated that the feeding of naturally-infected dung beetles (*Onthophagus taurus*, *Caccobius schreberi*, *Aphodius fimetarius* and *Sphæridium* sp.), as well as experimentally-infected *Blattella germanica*, to sheep, and of experimentally-infected *Blattella germanica* to calves and pigs, produces typical infections in the esophageal wall of the mammalian host. Once within the digestive tract of the definitive host, the larvæ probably burrow into the wall of the stomach or duodenum and migrate along the wall of the tube up to the esophagus or oral cavity. Baylis (1925) demonstrated that the larvæ do not migrate through the blood stream.

Further cross-experimental work of an extensive character is required in order to determine whether the gongylonemate nematodes from these several hosts are one and the same species, or whether there are morphological or physiological grounds for regarding at least some of them as closely related but distinct species.

Epidemiology.—Human infection with *Gongylonema* is both incidental and accidental. While the exact origin of the worms recovered from man is not known, it is possible that the larvæ were ingested in raw drinking water, into which infected intermediate hosts had fallen and were disintegrating.

Pathogenesis, Pathology and Symptomatology.—In non-human mammalian hosts the gongylonemate worms are found in burrows in the mucosa

...

of the worms migrating to the esophagus, which is the more usual habitat in ruminants. The patients harboring the parasites were conscious of their presence and of their migrations. In one case the worm may have been directly or indirectly responsible for an acute pharyngitis and stomatitis. In at least two of the patients severe nervous symptoms, which accom-

panied the presence of the worms, disappeared as soon as the parasites had been removed. It seems probable, therefore, that both local and indirect symptoms are produced by the presence of these worms in the oral mucosa or subdermal connective tissue. There is no evidence, however, that *Gongylonema pulchrum* produces neoplasms of the digestive mucosa such as *G. neoplasticum* and *G. orientale* of rodents have been found to do.

Diagnosis.—The presence of these thread-like worms actively migrating through subdermal tunnels of the oral cavity suggests the possibility of gongylonemate nematodes. Specific diagnosis can be made only after the worms have been removed and carefully examined under the microscope.

Therapeusis.—The worms may be removed by skillful insertion of a hooked needle under the worms when they come close to the surface in the region of the thin labial mucosa. In one case an antiseptic mouth wash containing thymol stimulated the worm to work its way out of its tunnel, so that it was easily removed with the fingers.

Control.—Infections in man, like those of other mammals, are probably acquired from accidental ingestion of infected insects, the cockroach, *Blattella germanica*, being the most likely human contact. However, the possibility must not be overlooked that larvæ migrate out of disintegrating cockroaches and may be swallowed in contaminated water. In human cases prevention is a matter of personal hygiene.

Genus Habronema Diesing, 1861

This spiruroid worm belongs to the type Family Spiruridæ, subfamily Spirurinæ. Adults are parasitic in gastric tumors of mammals and birds. Three species, *H. muscæ*, *H. megastoma* and *H. microstoma*, parasitize the horse and utilize *Musca domestica*, *Stomoxys calcitrans* and other filth flies, whose larvæ feed on horse manure, as intermediate hosts. Eggs laid by the female worms escape through openings in the tumor encasing the worms, pass down the digestive tract and are evacuated in the horse's feces. The embryos are ingested by the fly maggots, develop through three larval stages and survive in the tissues of the fly until it becomes adult. They then escape down the fly's proboscis onto mucous membranes, as the conjunctival epithelium, or into open sores on which the adult fly may feed. They produce habronemic ophthalmiasis in horses. Bull (1922) found suggestive evidence but no actual proof that the mature larval stage of a *Habronema* was responsible for a granulomatous tumor of 3 mm. outer diameter which was removed from the conjunctival epithelium of the upper left eyelid, near the external canthus, of a thirteen-months'-old child seen in the Adelaide, Australia, Hospital. Even in horses the ophthalmia is transient, since the larval nematode is not able to survive the rapid phagocytic action of host-tissue cells. Bull suggested that "bung eye" of natives of the Australian bush may be caused by this worm.

Family GNATHOSTOMATIDÆ R. Blanchard, 1895

The species of this family are characterized by having a cuticular cephalic bulb, provided either with conspicuous transverse striations or rows of posteriorly directed hooklets. The mouth possesses a pair of large trilobed lateral lips, with thickened cuticular surfaces, each member of the pair

being opposed to its mate. Opening into the peri-esophageal region of the head are the ducts of the two (or at times three?) pairs of long club-shaped cervical glands. The male has four or more pairs of papillæ supporting the caudal alæ, and two spicules. The vulva of the female is postequatorial; the vagina is directed anteriad. The females are oviparous. The eggs are thin-shelled and sculptured. Two species of the genus *Gnathostoma* (*G. spinigerum* and *G. hispidum*) have been reported from man.

Genus Gnathostoma Owen, 1836

(genus from γνάθος, jaw, and στόμα, mouth)

Gnathostoma spinigerum Owen, 1836.

Synonyms.—*Cheiracanthus robustus* Diesing, 1836; *Cheiracanthus siamensis* [illegible] 1890; *Gnathostoma siamense* (Levinsen, 1890) Railliet, 1893.

[illegible]

[illegible] obtained by Deuntzer from a breast abscess of a native woman from [illegible]

[illegible]
cases by [illegible]
cases by [illegible]
2 cases [illegible]
by Map[illegible]
Mukerji [illegible]
Morishi[illegible]
(1918) [illegible]
unfounded, since Heydon (1929) makes mention of *G. spinigerum* only in cats. More recently Toumanoff and Le-Van-Phung (1947) and Toumanoff and Nguyen-Van-Huong (1947) have diagnosed two cases of *Gnathostoma spinigerum* in Indochina, once in a native female of 42 years who may have contracted the infection in Thailand, and once in an Eurasian female of 22 years who had never lived outside Indochina. The only reference to human beings harboring the adult worms in the intestinal tract is that of Chandler (1927), who, on two occasions, found eggs of *Gnathostoma spinigerum* in examination of stools, presumably human, from Burma and Eastern Bengal, where the infection is common in cats. Thailand is the country of greatest prevalence of this worm, both in human and reservoir hosts.

Structure of the Adult Worm.—The adult worms in the type host (*Felis tigris*) reach a length of 11 to 25 mm. for males and 25 to 54 mm. for females. In dogs the worms are somewhat smaller and in cats even more restricted in size. The females are also stouter than the males. They are robust nematodes, reddish in color and slightly transparent, with a globular cephalic swelling separated from the rest of the body by a cervical constriction (Fig. 254 *B*). The oral end is frequently curved ventrad, while the posterior end is strongly recurved ventrad and inwards. In tumors of the

intestinal tract, the worms are tightly coiled within the cavity of the nodule, which contains one or more adult individuals.

The anterior half of the worm's cuticula is provided with leaf-like spines, which are most common in the area immediately behind [illegible] region and become less [illegible] anteriormost spines (Fig. [illegible] posteriormost ones are na[illegible] have only a single point. The posterior part of the body is entirely devoid of spines and the cuticle is entirely smooth. Superficial annular creasing of the body is common. The globular cephalic portion of the worm bears two large fleshy lips that guard the mouth. The head portion of the mature worm is covered with eight transverse rows of simple, sharply-pointed, recurved hooks (Fig. 254 *C*). The mouth opens directly into the esophagus (*es*), a large muscular tube,

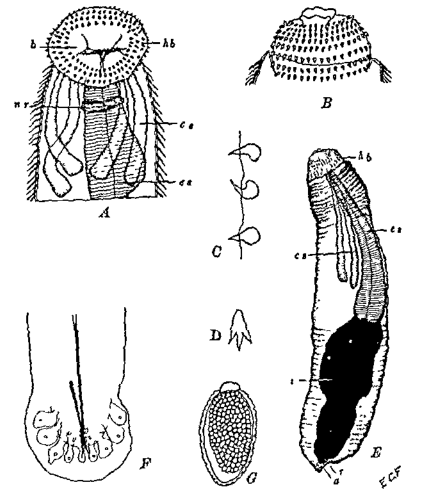


FIG. 254.—*Gnathostoma spinigerum* *A*, anterior end of immature worm showing cephalic [illegible]

[illegible] *cs*, cervical salivary glands of right side, *i*, intestine filled with food, *r*, rectum, *a*, anus, × 40 (adapted from Morishita and Faust, Journal of Parasitology). *F*, posterior end of male worm, ventral view, showing papillæ and spicules, × 40, (adapted from Baylis and Lane), *G*, partially embryonated egg of *G spinigerum*, from feces of naturally infected cat, × 333 (After Faust, Journal of Parasitology.)

which extends several millimeters posteriad and in young specimens (Fig. 254 *E*) may reach to the equatorial pane. This is followed by the intestine (*i*), which communicates posteriad with a short conical rectum (*r*), the latter opening through the anal pore (*a*) a short distance in front of the caudal tip (Fig. 254 *E*). Four large club-shaped cervical secretory glands (Fig. 254 *A*, *E*, *cs*) are arranged symmetrically around the esophagus. They lie in the body cavity and their ducts fuse in pairs on either side of the head to discharge through a common duct that perforates the adjacent lip

In the male (Fig. 254 *F*) the posterior end has a cuticular expansion surrounding the genital apparatus. There are four pairs of nipple-shaped papillæ around the cloaca. The spicules are unequal, solid, chitinous rodlets, measuring 1.1 mm and 0.4 mm. respectively. The vulva in the female worm lies a short distance behind the equatorial plane. There is a long, anteriorly directed vagina, which divides into two uterine tubes. The eggs (Fig. 254 *G*) are transparent ovoidal objects, with a sculptured or pitted shell and a mucoid plug at one pole. They measure 65 to 70 μ in length by 38 to 40 μ in transverse diameter and are in the unsegmented or 2-celled stage of development when oviposited

The Life Cycle of Gnathostoma.—The life cycle of *Gnathostoma spinigerum* has been elucidated only within recent years. According to Prommas and Daengsvang (1933) and Yoshida (1935), eggs are in the one- or two-celled stage when evacuated in the feces of the cat, which is the common domestic reservoir and in which the worms grow to maturity. Embryonation in water at 27°–31° C. requires about one week. Hatching then occurs of the motile, first-stage rhabditoid larvæ, which measure 223–275 μ by 13.4–17.4 μ and are provided with a rotund cephalic bulb beset with spines. These larvæ survive free in the water for only two or three days, but if they are meanwhile ingested by various species of Cyclops, they penetrate into the arthropod's hemal cavity and in 10 to 14 days transform into second-stage rhabditoid larvæ, measuring 350–450 μ by 60–65 μ and with a head bulb provided with four distinct rows of spines, as well as a functional digestive tract and two pairs of cervical glands like the mature worm.

Prommas and Daengsvang (1936, 1937) and Africa, Refuerzo and Garcia (1936) discovered independently that a second intermediate host is required. This may be a fresh-water fish (*Clarias batrachus*, *Monopterus albus*, *Ophiocephalus striatus* in Thailand, *O. striatus*, *Glossogobius giurus* and *Therapon argenteus* in the Philippines), a frog (*Rana rugulosa*, *fide* Daengsvang and Tansurat, 1938) or a snake (*Python reticulatus*, *Naja bungarus* and *N. tripudians*, *fide* Chandler, 1925). The adolescent worms are encapsulated in the muscles, liver, mesentery or other tissues of this host. They differ from adult *Gnathostoma spinigerum* in having only four instead of eight rows of transverse cephalic hooklets, and in this respect agree with the larval forms described by Morishita and Faust (1925) from peripheral lesions in the human host Chandler (*l. c.*) suggests that the worms only attain the full complement of cephalic hooklets after a final moult It is significant to note that the worms described by Leiper (1909) and Tamura (1921) from peripheral foci in man were provided with eight rows of cephalic hooklets, and in both size and structure were practically mature.

Prommas and Daengsvang (1937) fed the immature worms, obtained from fish hosts, to three uninfected cats. Two of these animals became positive on the 198th and 223rd day respectively after feeding and, when sacrificed later, each had a gastric tumor, in the hollow center of which adult *Gnathostoma spinigerum* were found.

Epidemiology.—In Nature the reservoir hosts acquire infection from consuming infected fresh-water fishes, frogs and snakes. As yet it is not known whether human infection results from this type of exposure or from the accidental swallowing of infected *Cyclops* in raw drinking water.

Fourteen of the 16 cases specifically reported from Thailand, 4 of the 5 from India, and one of the 4 from Japan and China were females and the remainder were males. In a majority of the cases reported by Prommas and Daengsvang (1934) there was a history of cats in the home.

Pathogenesis, Pathology and Symptomatology.—Lesions produced in the digestive tract, primarily in the stomach, have been described only from reservoir hosts. They consist of indurated nodules, formed of host tissue around one or more mature or maturing worms, which lie free in an abscess pocket in the center of the tumor. The worms are bathed with a milky purulent exudate. There is frequently a pore from this pocket opening into the intestinal lumen, through which eggs laid by the adult females are discharged. There is no evidence of malignancy in the tumor wall. This type of lesion is referred to as *gnathostomiasis interna*.

The lesions observed in the human host have been almost exclusively cutaneous or subcutaneous in anatomical position, and consist either of indurated nodules with abscessed centers or tunnels between the epidermis and corium, with infiltration of large numbers of eosinophils and lesser numbers of plasma cells. An infection consisting of such peripheral lesions [illegible] *externa*, and in the migrating variety [illegible] arva migrans") which requires differentiation from that produced by hookworms (*vide* pp. 435) or fly maggots (*vide* Cr [illegible]

[illegible] tion. Thirteen were nodular and eleven were [illegible] Localities in which the former occurred were the breast, pharynx, right side of face, axillary node, abdomen, ear (mastoid-like swelling), throat, forehead, finger of left hand, right side of chest, right thenar eminence, intra-orbital and anterior chamber of the eye. The creeping eruption type was almost always within the deeper layers of the skin. A majority of the histories indicate that symptoms appeared for the first time only a few days before a physician was consulted, but some cases of "larva migrans" had remained active for two to seven years (Prommas and Daengsvang (1934). Maplestone [illegible] (1937) characterize the lesion in the human subject as follo[illegible] circumscribed swelling, with or witho[illegible] subsiding in a few days, at times with recurrence [illegible] near-by or distant site; hematemesis, hemoptysis or hematuria rarely appearing concurrently and subsiding on removal of worm; occasionally with an associated suppuration and abscess formation, pruritus present only in superficial lesions, edematous swelling somewhat resembling

angioneurotic edema more typical; eosinophilia relatively characteristic. Toumanoff and Le-Van-Phung (1947) call attention to the eosinophilia and pronounced lymptocytosis frequently attendant on infection with *G spinigerum*.

The case of ophthalmic involvement reported by Sen and Ghose (1945) included a history of moderately sudden development of a dull aching pain on the left side of the nose, extending to the left frontal and temporal regions. Swelling of the face occurred, followed by orbital cellulitis, with hemorrhage in the vitreous and retina Following four attacks of iritis a pigmented nodule was seen on the iris Inflammation of the region disappeared with removal of the nodule but optic atrophy developed. The nodule contained an immature *Gnathostoma*, having a length of 3.5 mm., a maximum width of 0.41 mm. and four rows of head spines

Diagnosis.—Specific diagnosis can only be arrived at after removal of the worm and study of its peculiar structure, although inflammatory cutaneous swellings with marked eosinophilia, and a history of residence in endemic areas may suggest the presence of this helminth in the lesion (Castens, 1935).

Therapeusis.—In *gnathostomiasis externa*, this consists in excision of the worm with its surrounding abnormal tissue. Therapeutic procedure for *gnathostomiasis interna* has not been studied

Control.—No statement with respect to prophylaxis can be made until the epidemiology has been further elucidated. It seems altogether likely that man is not the optimum host of the worm It is problematical whether the infective-stage larvæ enter the human body *via* the skin or *via* the mouth, although the latter route is the common one for reservoir hosts

Gnathostoma hispidum Fedtschenko, 1872.

hi

and domesticated pigs in Central and Eastern Europe. It has also been reported from this host from Turkestan, India,
Rabaul, New Guinea It has been found
infection has been described from Tokyo,
the left thenar eminence. A young female worm was removed from the lesion.

caudal extremity, and in having only one pair of small, ventral, alar papillæ on the male

The clinical aspects of *gnathostomiasis hispida*, in general, resemble those of *gnathostomiasis spinigera*

Family PHYSALOPTERIDÆ Leiper, 1908

ends. The vulva of the female is preequatorial. The eggs are transparent, thick-shelled objects and are embryonated at time of oviposition. Studies by Ortlepp (1926) *indicate that only one member of this family has thus* far been found as a human parasite.

Genus Physaloptera Rudolphi, 1819

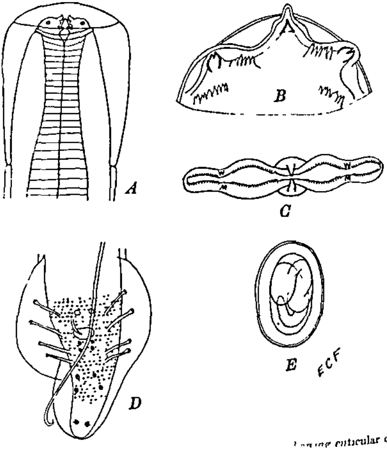
(genus from φυσαλίς, bubble, and πτερόν, wing)

Physaloptera caucasica v. Linstow, 1902.

Synonym.—*Physaloptera mordens* Leiper, 1907.

Historical, Geographical and Biological Data.—This nematode was first obtained by Ménétriés from the ileum of a patient in the Caucasus (v. Linstow, 1902). It was also obtained by Leiper (1907) in a native child in Uganda. Later Leiper and Turner (Leiper, 1913) found it to be quite common in natives of Tropical Africa. Blackie (1932) has reported this species from a patient, as well as from monkeys and the baboon in Southern Rhodesia. Faust and Martinez (1935) found *Physaloptera* eggs in the feces of a native of Panamá, but concluded that it was a case of spurious parasitism.

The worm lives attached to the wall of the intestine all the way from the esophagus to the ileum. Turner has also recovered occasional specimens from the liver. Leiper believes monkeys, which harbor the infection in Africa, are the reservoir hosts.



... cuticular collarette,
lips, ... of male worm, showing asymmetrical alæ, pedunculated and sess... × 375 (After ...
(adapted from v. Linstow), *E*, embryonated egg of *P. caucasica*,
Annales de Parasitologie).

The worms are of considerable size, the males measuring 14 to 50 mm. in length by 0.7 to 1.0 mm in breadth and the females, 24 to 100 mm by 1 14 to 2 8 mm In

, but are

ry grad-

arp tip

The anterior end (Fig. 255*A*) is surrounded by a reflected portion of the cuticula, which forms a collarette around the head The mouth is surrounded by two fleshy lips, which are oblong in shape and lateral in position (Fig 255*B*, *C*) Each lip is provided on its median aspect with a series of dental processes, consisting of a middle single-pronged tooth which is immediately apposed to a similar prong from the other lip, two double-pronged teeth similarly apposed, and a considerable number of intermediate minute denticles Each lip also bears two conspicuous submedian papillæ, the four papillæ being situated in a quadrangular position

The bursa copulatrix (Fig 255*D*) is composed of asymmetrical alæ, of which the right member is shorter and slightly broader, and the left member passes around the caudal extremity and terminates just in front of the posterior margin of the right Typically there are 4 pairs of pedunculate papillæ and 6 pairs of sessile or subsessile ones, arranged as in the accompanying diagram (Fig 255*D*) An additional preanal pair may also be present The pericloacal cuticula is transversely bossed. The spicules are unequal capillary rods, gradually tapering distally to a point, and commonly curled distally The left one has a length of 3 2 to 5 5 mm. and the right one, of 0.476 to 0 62 mm

The vulva of the female opens in the vicinity of the posterior limit of the esophagus The vagina leads posteriad, becoming swollen in its more distal portion into an egg chamber Just behind this region it reflexes on itself and soon bifurcates twice to form four uterine tubules Two of these uteri with their oviducts and ovarian tubules are situated anteriorly and two, posteriorly The eggs (Fig 255*E*) are smooth, thick-shelled, transparent, ovoidal objects, having a range in measurement of 44 to 65 μ (length) by 32 to 45 μ (breadth) The eggs *in utero* contain mature larvæ

The life cycle of *Physaloptera caucasica*, like that of other species of this family, is unknown, but it is believed that insects or other arthropods serve as intermediate hosts

Clinical Data.—The clinical aspects of this infection have not been studied

Control. Unstudied

Family THELAZIIDÆ Railliet, 1916

Members of this family lack definite lips but usually possess a short buccal capsule The caudal end of the male is conspicuously recurved and may or may not have alæ but is usually provided with preanal and at times postanal papillæ The eggs, when laid, are fully embryonated. Adults live in the orbital, nasal or oral cavities of mammals and birds, in the air-sacs of birds, or in the intestine of fishes. An intermediate insect host is probably required. Two species of the type genus, *Thelazia*, have been reported from man

Genus Thelazia Bosc, 1819

(genus from θηλάζω, to suck)

Thelazia callipæda Railliet and Henry, 1910 (The Oriental "eye worm," producing thelaziasis)

Synonyms. *Filaria palpebralis* of Houghton, 1917; *Filaria circumocularis* of Ward, 1918.

Historical and Geographical Data.—This worm was first described by Railliet and Henry (1910) from a single female specimen, recovered from the nictitating membrane of a dog in Rawal Pindi (Punjab). Since that time it has been found many times in the conjunctival sac of dogs in the Punjab, Burma, Central and North China. It has been recovered as a natural infection of cats in Peiping (North China), Chengtu (West China) and Kweiyang (South China), respectively by Hsu and Li (1941), Lu (1941) and Chin and Li (1942). It has been recorded once as a natural infection in the rabbit (Faust, 1927). There are six records of *Thelazia callipæda* in man, consisting of five infections with the adult worms in the conjunctival sac (Stuckey, 1917, in a Peking coolie; Trimble, 1917, in a Fukienese farmer; Hsu, 1933, in a Chinese boy of ten years at Changhsintien, Wanpinghsien, North China; Chin, 1942, in a young male, native of Hua Hsien, Kwanghsi Province, China, and Nakata, 1934, in a Korean girl), and one with larvæ in an advanced stage of development attached to the epithelial layer of a wart-like papilloma of the lower eyelid of a western physician in Chengtu, Szechuan (Howard, 1927). Barlow's report (1921) of a living *T. callipæda* recovered from the stool of a Chinese patient after anthelmintic treatment appears to be a case of inaccurate identification (Faust, 1928, Hsu, 1933). Friedmann (1948) has recorded the first human infection of *T. callipæda* in India, in a 15-months'-old native female.

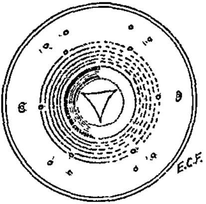


FIG. 256.—*Thelazia callipæda.* Head-on view, showing distribution of perioral papillæ, × 6 (Adapted from Hsü, 1933, in Craig and Faust's Clinical Parasitology.)

Structure of the Adult Worm.—The adult worms are creamy- or ivory-white in color, cylindrical in shape and tapering at both ends; they range in size from 4.5 to 13 mm. by 0.25 to 0.75 mm. for males and 6 to 17 mm. by 0.3 to 0.85 mm. f ... cuticula is plaited into well-defined transverse str ... edges. The oral end ... each with a single nerve terminus; four twinned submedian papillæ, ... pair of lateral amphids (Hsü, 1933). (*Vide* Fig. 256.) The buccal capsule (Fig. 257 *A*) presents the appearance of being discontinuous ventrally but Hsü states that it is continuous.

The male (Fig. 257 *B*) has a conspicuously recurved posterior end. There are 6 to 10 pairs of sessile, preanal papillæ and 2 to 3 (possibly 5) similar pairs in a postanal position. The copulatory spicules are two in number, one being short and rigid, slightly twisted, club-shaped, with curved lateral alæ along the entire length, and one, very long, rod-shaped and commonly less rigid. The vulva of the female opens ventrally, some

distance behind the equatorial plane of the esophagus. The vagina is directed posteriad, as is the outer portion of the uterus, which originates as a single stem just behind the ovejector, internally dividing into two arms, which parallel one another in complicated coiling in the posterior half of the body. The corresponding oviducts and ovaries are also situated in the posterior part of the worm. The eggs are embryonated when laid, are at first ovoidal and measure 54 to 60 μ by 34 to 37 μ, but their capsule soon enlarges into a spherical surface, with a finger-like evagination on one side, into which the larva crawls. The life cycle of the worm has not been elucidated but an intermediate arthropod host is probably required, as

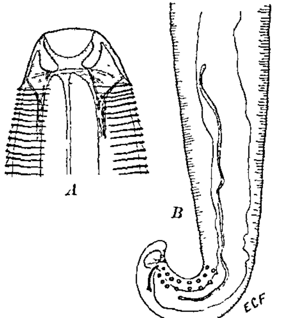


FIG 257 — *Thelazia callipaeda.* *A*, anterior end of worm, showing buccal capsule and cuticular plaiting, × 350, *B*, posterior end of male worm, showing preanal and postanal papillæ and copulatory spicules, × 55 (After Faust, Journal of Parasitology)

has been demonstrated for the "eye worm" of the fowl, *Oxyspirura mansoni*, which passes its intermediate stage in a cockroach. When a chicken eats an infected cockroach, the encapsulated larvæ of the worm are liberated, migrate up the esophagus, pharynx and lacrymal duct, and emerge into the inner canthus of the eye

Epidemiology.—Incompletely elucidated. In restricted endemic foci in and near Peiping, China, dogs become reinfected each spring or early summer It is more prevalent in dogs and cats in South China than in the north of the country.

Pathogenesis, Pathology and Symptomatology.—The worms live in the conjunctival sac of the host. Ordinarily they produce little conjunctivitis but stimulate a secretion of lacrymal fluid. In dogs which become reinfected every summer the surface of the eyeball becomes gradually opacified by the intermittent gliding of the worms across its surface Movement of

the adult worms over the eye ball may possibly be responsible for paralysis of the muscles of the lower eyelid and cause ectropion (Trimble, 1917). The presence of the worms in the conjunctival sac is accompanied by intense pain and gives rise to extreme nervous symptoms.

Diagnosis.—The creamy-white thread-like worms which crawl out from the conjunctival sac over the eyeball may be removed with eye forceps and examined under the microscope.

Therapeusis.—Instillation of 2 per cent cocaine solution into the conjunctival sac of an infected member will cause the worms to crawl out of the canthus of the eye, allowing their removal with eye forceps within a few minutes.

Control.—Since man is only an incidental host, while dogs and cats are the reservoirs of the infection, human beings presumably acquire the infection through association with infected dogs, although direct infection is probably not possible. Periodic removal of these worms from the eyes of dogs and cats should reduce the hazard of human infection.

Among the 10 or more species of *Thelazia* described from mammals and 10 from birds (Price, 1931), only one other, *T. californiensis* Kofoid and Williams, 1935, has been reported as a human parasite. It has been recovered once from man (Kofoid and Williams, 1935; Hosford, Stewart and Sugarman, 1942), several times from dogs, once from a cat, once from a sheep, once from a black bear, from the Columbian black-tailed deer (*Odocoileus hemionis columbianus*) an[illegible]
(Herman, 1944). This species is sta[illegible]
arranged pairs of preanal papillæ and [illegible]

Family ACUARIIDÆ Seurat, 1913

A species of spiruroid worm (*Cheilospirura* sp.), belonging to the family Acuariidæ Seurat, 1913, has been reported by Africa and Garcia (1936) from an ovoidal tumor mass, situated on the lower palpebral conjunctiva, about 1 cm. from the external canthus of the right eye of a Philippine farmer, who had been suffering from a chronic catarrhal conjunctivitis and keratitis of the organ.

CHAPTER XXIX

PHASMID NEMATODE PARASITES OF MAN (CONCLUDED)

SUPERFAMILY FILARIOIDEA (WEINLAND, 1858) STILES, 1907
(FILARIOID FORMS)

THIS superfamily comprises those spirurate nematodes of filiform outline, having a simplified anterior end, without conspicuous oral labia. The buccal vestibule is lacking or inconspicuous. The esophagus is cylindrical, without a cardiac bulbus, with or without differentiation into two parts. The mid-intestine is simple and may be atrophied posteriorly. In some species the male worms possess caudal alæ, in others these are lacking. The copulatory spicules are commonly unequal and dissimilar. The vulva of the female worms is preequatorial, usually in the esophageal region. The species of this group have become adapted to a habitat in the subcutaneous and deeper tissues of the vertebrate body, including the circulatory, lymphatic, muscular, and connective-tissue layers, or the serous cavities.

Typically the organism which is deposited by the female worm is an advanced-stage embryo, the *microfilaria*, which may have a "sheath" (*i. e*, the old egg shell elongated to accommodate itself to the uncoiled embryo), or it may be "sheathless" (*i. e.*, escaped from the egg shell). This microfilaria comes to circulate in the peripheral blood (or at times in the peripheral lymphatic vessels). When taken up by an appropriate blood-sucking arthropod, it proceeds to transform into a first-stage rhabditoid larva and then metamorphoses gradually into a filiform infective-stage larva. These larvæ then migrate out of the tissues down the proboscis sheath and are deposited on or in the skin of the vertebrate host when the arthropod prepares to take a blood meal. An arthropod intermediate host is required.

Filarioid species are classified under four families, **Filariidæ**, Claus, 1885, **Acanthocheilonematidæ** Faust, 1939, **Desmocercidæ** Cram, 1927 and **Stephanofilariidæ** Wehr, 1935. The species parasitic in man all belong to the

Family ACANTHOCHEILONEMATIDÆ Faust, 1939

(Synonyms: *Dirofilariidæ* Sandground, 1921; *Dipetalonematidæ* Wehr, 1935)

In this family the females are not more than three or four times as long as the males. The anal opening is constantly present in both males and females. The cuticula is usually smooth, but may be characterized by transverse striations, annular thickenings or bossing. The mouth is circular or dorsoventrally elongated; the cephalic papillæ consist of an external ring of 8 and an internal ring, if present, only of internolaterals. The esophagus may be differentiated into two morphologically distinct portions. The caudal alæ in the male are either very narrow or are lacking; the copulatory spicules are typically unequal and dissimilar. The female discharges slender, aspinose, microfilariæ (a pre-larval stage).

Subfamily Acanthocheilonematinæ Faust, 1939

(Synonyms: *Onchocercinæ* Leiper, 1911, *pro parte; Loainæ* Yorke and Maplestone, 1926, *pro parte; Setariinæ* Yorke and Maplestone, 1926, *pro parte; Dipetalonematinæ* Wehr, 1935)

Members of this subfamily either lack caudal alæ in the male or have extremely narrow alæ. Human representatives: *Wuchereria bancrofti* (Cobbold, 1877), *W. malayi* (Brug, 1927) Rao and Maplestone, 1940, *Onchocerca volvulus* (Leuckart, 1893), *Acanthocheilonema perstans* (Manson, 1891), *A. streptocerca* (Macfie and Corson, 1922) Peel and Chardome, 1946, and *Mansonella ozzardi* (Manson, 1897) Faust, 1929.

Genus Wuchereria daSilva Araujo, 1877

(genus named for Dr. O. Wucherer)

Wuchereria bancrofti (Cobbold, 1877) Seurat, 1921. (Bancroft's filaria, producing wuchereriasis bancrofti or Bancroft's filariasis.)

Synonyms.—*Filaria sanguinis hominis* of Bush, 1872; *Filaria sanguinis hominis ægyptiaca* Sonsino, 1874; *Filaria bancrofti* Cobbold, 1877; *Wuchereria filaria* da Silva Araujo, 1877; *Filaria wuchereri* da Silva Araujo, 1878; *Filaria sanguinis* v. Beneden, 1878, *Filaria nocturna* Manson, 1891; *Filaria philippinensis* Ashburn and Craig, 1906.

Historical Data—The pathological picture produced by Bancroft's filaria, consisting of elephantiasis of the leg and scrotum and, to a certain extent, lymph scrotum, was undoubtedly observed and described by ancient Hindu savants (600 B. C.), as well as by Rhazes, Avicenna and other Persian physicians, although the disease (*elephantiasis arabum*) was frequently confused with leprosy (*elephantiasis græcorum*) as well as with Madura foot. Hematochyluria was first described by Chapotin in 1812. Meanwhile many workers in Brazil (1800–1854) had been studying the various clinical expressions of the infection.

In 1863 Demarquay in Paris first demonstrated microfilariæ in hydrocele fluid of a patient from Havana, and in 1866 Wucherer made a similar discovery in chylous urine of a Brazilian patient (first published in 1868). In 1872 Lewis in India published his discovery of the same organism in the peripheral blood of a Hindu. In 1874 Sonsino described microfilariæ in the blood and urine of a Jewish lad in Egypt.

The first adult worms (five in number all females) were recovered by the elder

found metamorphosis; the second (1879) consisting in a demonstration of the nocturnal swarming (periodicity) of the
diurnal concentration in the pulmon
confirmed by Lewis and by da Silva
discovery.

been those of Bahr (1912) in Fiji, O'Connor (1920) in Ellice, Tokelau and Samoa, Anderson (1924) in British Guiana, numerous workers in India, and O'Connor and his associates (1929–1938) in Puerto Rico and the Virgin Islands

During the period 1942–1944 American military forces in considerable numbers were exposed to Bancroft's filariasis on several South Pacific island groups, *viz*, Samoa, Tokelau, Ellice, Tonga and Fiji An epidemic of early-stage manifestations of this infection developed in approximately a fourth of these troops. This lead to intensive epidemiologic and clinical studies which have added appreciably to a knowledge of the sources of exposure, pathogenesis and early symptoms of the disease.

Geographical Distribution of Bancroft's Filaria.—In general, it may be stated that, *Wuchereria bancrofti* occurs indigenously throughout the world from about 41° north to about 28° south latitude in the Eastern Hemisphere and from about 30° north to about 30° south latitude in the Western Hemisphere. (See map, Fig. 258.) It is believed that the infection originated in Southern Asia, from which it spread, on the one hand, through Malaya to Micronesia, Melanesia and Australia and through India to Southern and Central China and Japan; and on the other hand, through Africa to the Americas

In Asia it is found along the whole of the southern coast from Arabia through India, Burma, Siam, the Malay States, French Indo-China, Southern and Central China up to Southern Shantung Province, China, and *via* the coastal islands of the China Sea to Southern Korea and the southern half of Japan It is found in Sumatra and Java, in Borneo, Celebes, Flores, Soemba, Timor and the lesser islands of Indonesia, the Philippines, New Guinea and Papua, the Solomon Islands, and from Port Darwin in the Northern Territory, Australia, along the coast eastwards and southwards through Queensland to the northern part of New South Wales. It is extremely common in Fiji, Samoa, in the Gilbert and Ellice Islands and other parts of Micronesia, where the non-periodic variety of *W bancrofti* is transmitted by day-biting mosquitoes

In Africa it is frequently encountered along the East Coast from Eritrea to the mouth of the Zambesi and on the neighboring islands of Madagascar, Mauritius and Reunion. In North Africa it has a coastal distribution from Lower Egypt to Morocco. In Central Africa the infection is contiguous with the disease on the East though

...ungary, Jugoslavia, and in Turkey

In the United States the one previously known endemic area, that around Charleston, South Carolina, has become filaria-free.

It is of common occurence among the peoples of the Caribbean, including Cuba, Jamaica, Puerto Rico, Martinique and St. Kitts. It occurs in Panama, Columbia, Venezuela, the coastal portion of the Guianas (French Guiana, 12 to 18 per cent, Dutch Guiana or Surinam, 3 to 60 per cent depending on the social and economic strata), in Bahia, Belem and other areas of northern Brazil.

Some of the above records possibly refer to *Acanthocheilonema perstans*, *Wuchereria malayi*, *Mansonella ozzardi*, *Loa loa* or other *filariæ* having an overlapping distribution.

Stolls' estimate (1947) of the combined world incidence of *W. bancrofti* and *W. malayi* is 189 millions, of which 9 millions are allocated to Latin America, 22 millions to Africa, 157 millions to Asia and 1 million to the Pacific islands.

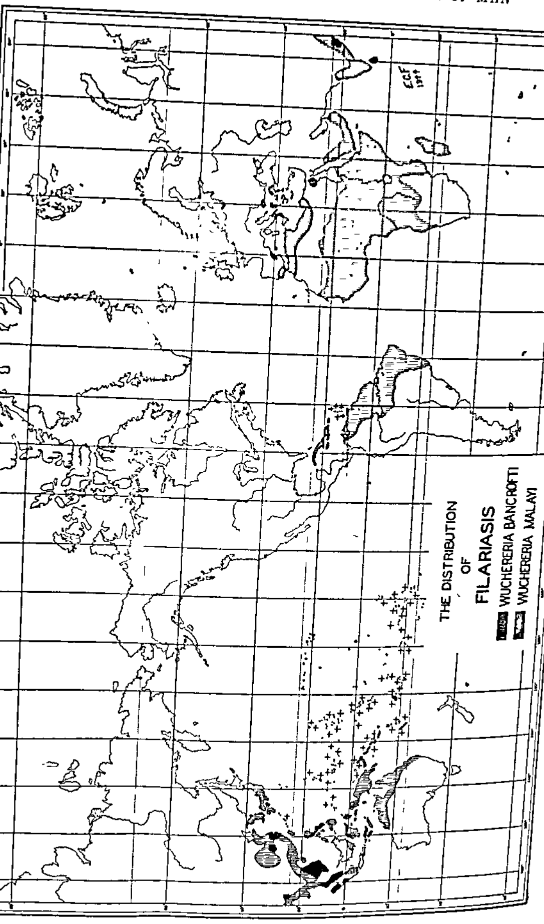


Fig 258 —Map showing the distribution of *Wuchereria bancrofti* and *W. malayi*, + ...
Pacific (Original by Faust, in Cr...

Morphology and Life Cycle of the Parasite.—*The Adult Worm.*—The adult specimens of *Wuchereria bancrofti* are creamy-white, filiform worms, with smooth cuticula and a cylindrical shape; they gradually taper towards both ends, which terminate bluntly. The head (Fig. 259 *A*) is slightly swollen and is provided with two rows of small, sessile papillæ The mouth is unarmed and there is no buccal vestibule. The oral aperture leads directly into a cylindrical esophagus of moderate length, divided into an anterior muscular part and a posterior glandular portion. The mid-intestine is a tube of one-third to one-fifth the diameter of the body of the worm. It opens into a short rectum in the plane where the worm begins to narrow posteriorly

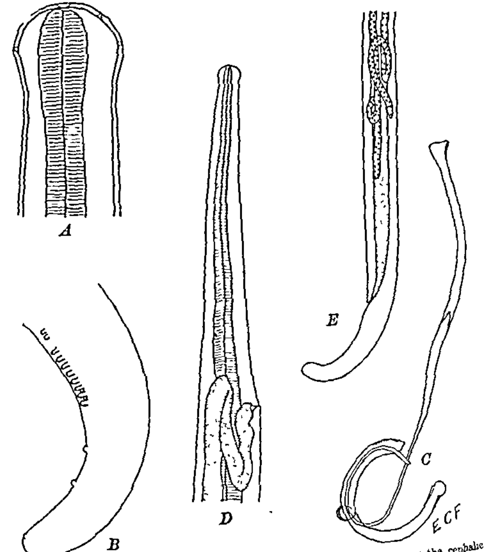
The male measures about 40 mm. in length by 0.1 mm. in cross-section. *The caudal extremity (Fig. 259 B) is curved sharply ventrad, at times* through an angle of 360 degrees. According to Leiper (1913), there are 12 pairs of sessile circumanal papillæ, of which 8 pairs are preanal and 4 immediately postanal in position. Maplestone (1929) states that these papillæ support very narrow, inconspicuous alæ. Farther caudad there are 2 pairs of rather large sessile papillæ, and at the caudal extremity a solitary pair of minute size. The present author has confirmed Leiper's *description from material secured from Central China.* There are two copulatory spicules (Fig. 259 *C*) of unequal length (0.2 mm. and 0.6 mm. respectively), the longer one being cylindrical and tapering distally to a long lash with delicate alæ and ending in a spoon-like termination, the shorter one being trough-shaped, having a uniform thickness, and being *provided with coarse markings near its distal end. The gubernaculum* is crescent-shaped.

The female measures from 80 to 100 mm. in length by 0 24 to 0.3 mm. in cross-section. The vulva (Fig. 259 *D*) opens about 0.8 to 0.9 mm. behind the anterior extremity of the body. The swollen vagina is about 0.25 mm. long and leads into a uterus which shortly divides into two branches. These tubules, having a diameter about three times that of the [illegible] of the body. [illegible] of the caudal [illegible] eri are coiled [illegible] at 38 by 25 μ. As they become crowded more and more towards the outer portion of the uteri, the membranes elongate to form a "sheath" encasing the microfilariæ but somewhat longer than the enclosed organisms, so as to allow room for the microfilariæ to slip back and forth within the "sheath." It is in this form that the embryos ordinarily escape from the parent worms. Usually described as viviparous, this condition is actually one of oviparity, since the membranes surrounding the embryos are the original egg capsules laid down by the parent and not cuticular sheaths secreted by the embryos themselves.

The adult worms live normally in the lymphatic vessels and the lymph glands, the microfilariæ, on escaping from the gravid females, may either remain in the lymph or migrate into the blood stream. In case female worms are injured, the embryos may possibly be discharged in the immature

ovoidal condition, under which circumstances they are too broad to pass the lymph capillaries. Manson attached considerable importance to this phenomenon as an explanation for the obstruction of the lymphatics frequently associated with the infection, but more recent investigators offer a different explanation. (*Vide infra*, pp. 505–506.)

The *microfilariæ*, *i. e.*, the embryos of *Wuchereria bancrofti* (Fig. 260), which are recovered from the peripheral blood or the lymph current, or are discharged in chylous urine, are minute serpentine organisms, measuring *127 to 320 μ in length by 7.5 to 10 μ in diameter.* Those in the lymph vessels are usually considerably shorter and slightly thicker than the ones that have escaped into the circulating blood or urinary tract. They are bluntly rounded at the anterior end and attenuate posteriorly. Abe (1935)



showing the cephalic

FIG. 259.—*Wuchereria bancrofti.* *A*, ante papillæ, × 400; *B*, posterior end of male, with worm; *D*, anterior end of female, lateral view, × 90. (*A*, *D*, *E*, after Yorke and Maplestone, N---- Leiper, Trans Royal Soc. of Med. and Hyg)

has described four small, equidistant papillæ on the cephalic end of the micr... The cuticula is usually described as having delicate transverse striat... depo... *W. bancrofti* and other common blood and tissue filariæ possess annular transverse cuticular striations that completely cover the embryos from tip to tip." The worms move about gracefully in a blood-film, pushing the blood corpuscles to one side. In living embryos the oral end is being constantly covered and uncovered by a prepuce; it is also described as being provided with a delicate stylet which may be introverted or everted as occasion requires.

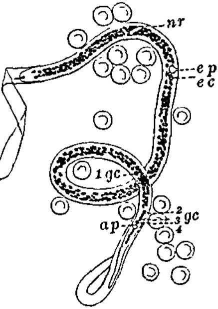


FIG. 260.—Ensheathed microfilaria of *W. bancrofti*, with oral stylet. *nr*, nerve ring, *ep*, excretory pore, *ec*, excretory cell, 1, 2, 3, 4, *gc*, so-called "genital cells"; *ap*, anal pore. × 666. (Original.)

The inner structure of the microfilaria cannot be clearly seen without the aid of staining. (For methods of staining see Chapter XXXIII, pp. 575–578.) *With either vital dyes or permanent stains the central axis of the microfilaria* will be found to be composed of a column of deeply-staining nuclei but certain landmarks can be found. These consist of the nerve ring (*nr*) in the anterior portion of the worm, an excretory pore (*ep*) and an adjacent excretory cell (*ec*) a short distance behind the nerve ring, so-called "genital cells" or G-cells (1-*gc*, 2-4-*gc*) in the posterior part of the organism, the latter three cells being situated close together in front of the anal pore (*ap*). The relative distances of these landmarks from one another along the ... relation of length to breadth, ... *so, since they are constant in* the same species ... relative percentage distance of

these locations from the anterior extremity, according to Fulleborn and Rodenwaldt, is: nerve ring, 20; excretory pore, 29.6; excretory cell, 30.6; G-cell 1, 70.6; anal pore, 82.4; with G-cells 2, 3 and 4 situated far behind G-cell 1 and immediately in front of the anal pore. Likewise the terminal 5 per cent of the microfilaria of *W. bancrofti* is free of nuclei. This latter important character makes it easy to distinguish it from the similar stage of *W. malayi* and *Loa loa*, in which the nuclei extend to the caudal extremity. (*Vide* Table 3.)

Microfilarial Periodicity.—In 1877 Manson first found in his China cases showing microfilariæ that the maximum concentration of these embryos in the peripheral blood occurred at night. This observation of the nocturnal periodicity of microfilariæ of this species has been reported consistently since that time in autochthonous infections in China, India, the islands of the Southwest Pacific, Australia and the West Indies. The maximum concentration in the peripheral circulation is normally between 10 P.M. and 2 A.M., while in the daytime Manson found the embryos concentrated in the pulmonary vessels, the capillaries of the heart muscles and the Malpighian tufts of the kidneys. On the other hand, autochthonous cases in the Philippines, and more particularly in Fiji, Samoa, Tokelau, Wallis, and Ellice Islands and Tahiti, which have an infection consisting of adults and microfilariæ morphologically indistinguishable from the Asiatic, Australian and West Indies strains and which are considered to be the same species, lack specific periodicity (*i. e.*, are non-periodic).

In a study of the periodicity of microfilariæ of *W. bancrofti* from patients who contracted the infection in the Pacific area, Eyles, Hunter and Warren (1947) state that (1) west of 140°E. Longitude only nocturnal periodicity occurs; (2) between 140°E. and 180°E. Longitude both periodic and non-

TABLE 3.—DIFFERENCES BETWEEN MICROFILARIA BANCROFTI, MF. MALAYI and MF. LOA (ADAPTED FROM FENG, 1933)

	Mf bancrofti	*Mf malayi*	*Mf. loa*
1	Periodicity usually nocturnal	Periodicity nocturnal	Periodicity diurnal
2	Length: 244 to 296μ (thick films)	Length. 177 to 230μ (thick films)	Length: 250 to 300μ (thick films)
3	Excretory cell small (30 75%), near excretory pore (28 95%)	Excretory cell: large (37 07%), far behind excretory pore (30.9%)	Excretory pore: similar (36 6%) to *Mf malayi* (31 6%)
4.	G-cells. small, similar size; G_2–G_4 far behind G_1; G_1, 70 14%	G-cells: larger; G_1 relatively near and larger than G_2–G_4; G_1, 68.33%	G-cells. similar to *Mf malayi*, G_1, 68 6%
5.	Anal pore: 82 48%	Anal pore 82 28%	Anal pore. 81 9%
6	Tail: tapering to delicate point; no terminal nuclei	Tail: swollen at levels of 2 terminal nuclei	Tail. tapering gradually; caudal nuclei continuous with those of the trunk
7.	Appearance: graceful, sweeping curves	Appearance: stiff, with secondary kinks	Appearance. similar to *Mf. malayi*
8	Pathology: elephantiasis of lymphatics of scrotum as well as extremities	Pathology: confined mostly to lymphatics of upper extremities	Pathology: fugitive swelling of subcutaneous tissue
9	Intermediate hosts: optimum, *Culex quinquefasciatus*, *Aëdes* spp., *Anopheles* spp.	Intermediate hosts: *Mansonia* spp., *Anopheles* spp	Intermediate hosts: *Chrysops* spp

periodic varieties are present, and (3) east of 180°E. Longitude only the non-periodic type is found. It is suggested by these workers that "non-periodic" is an inappropriate term, since there are actually a relative "low" and a relative "high" in the number of microfilariæ during any twenty-four-hour period. Similarly, it may be pointed out that "periodic" is a relative term, since a few microfilariæ can usually be found in cutaneous blood vessels during the day-time hours of patients infected with the "periodic type"

The theories that have been advanced to explain periodicity are primarily based on mechanical, chemical or biological processes. It was first supposed that the period of sleep and the relaxation of the capillaries at night or contraction during the daytime were responsible for the condition, but this theory fails to explain non-periodicity. The dilatation of lymphatic capillaries at night, carrying the embryos into the blood stream, is subject to the same criticism. Chemotactic responses to oxygen and carbon dioxide gases have also been advanced as an explanation without any considerable valid evidence. Harley (1932) stressed the chemotactic response of the embryos to the salivary secretion of the insect intermediate host, introduced

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a nocturnal periodicity, whereas non-periodicity occurs where a day-feeding mosquito, such as a species of *Aedes*, is utilized. It is argued, however, that these observations are entirely too isolated and without confirmation in other endemic areas to explain satisfactorily the intermediate host-parasite relationship of this species on the basis of adaptation alone. Lane (1929, 1933) believed that the simultaneous development of the embryos and mid-day parturition of the mother worms, as demonstrated by O'Connor (1931), provides new microfilarial progeny which require approximately twelve hours to reach the peripheral circulation Lane's correlated hypothesis, that the microfilariæ survive only twenty-four hours, has been conclusively disproved by Rao (1933) *in vitro* and by Knott (1935) in uninfected human volunteers, in whom the microfilariæ survived for at least two weeks after inoculation.

Khalil (1939) has called attention to the positive thermotropism of both the adult worms and the microfilariæ of this species. Furthermore, the adult *W. bancrofti* are usually located in the lower extremities and genital organs and their microfilariæ have a much longer journey to the blood stream than have the *Mf. malayi*, which more frequently originate in the upper extremities. Since a maximum flow of chyle occurs about midnight, it follows that the maximum surge of *Mf. bancrofti* into circulating blood should take place at this time.

The following observations have a bearing on one or another of the theories proposed. In persons sleeping during the daytime the microfilariæ have a diurnal periodicity, although Yorke and Blacklock (1917) found that

it required eleven days for a complete reversal in periodicity in a person changing from nocturnal to diurnal sleep. Persons harboring a strain manifesting nocturnal periodicity may move their residence to a country where only the non-periodic strain is endemic without causing a modification of the periodicity. In Australia various observers have found that during the winter months when *Culex quinquefasciatus* disappears, there is not only a marked decrease in the percentage of cases in whose peripheral blood the microfilariæ occur, but there is a distinct diminution in the actual number of microfilariæ found in films of peripheral blood of positive cases.

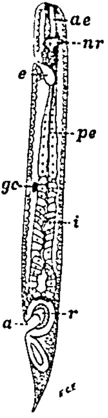
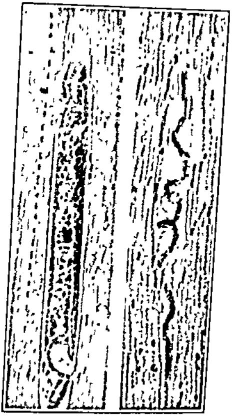


FIG. 261



A FIG. 262. B

FIG. 261.—Sausage-shaped larva of *W. bancrofti* from thoracic muscles of *Culex pipiens*. *ae*, anterior esophagus, *nr*, nerve ring, *e*, excretory bladder, *pe*, posterior esophagus, *gc*, genital primordium, *i*, mid-intestine, *r*, rectum; *a*, anus. × 300 (Original)

FIG 262.—*A*, Photomicrograph of sausage-shaped larva of *W. bancrofti* in *Culex pipiens*; *B*, photomicrograph of mature larva in *Culex pipiens* (Photographs by Dr. C. U. Lee)

Altogether the evidence for one or the other of these theories is still unsatisfactory and unconvincing, and further intensive investigations on both the periodic and non-periodic strains of the organism are needed in order to throw light upon this perplexing question.

The Mosquito Intermediate Host.—In 1878 Manson demonstrated that that *Culex "fatigans"* served as a "nurse" for the microfilariæ of the China strain of

filariæ pas

"exsheath

feces, but

hours, migrate into the thoracic muscles, where their movement becomes greatly reduced. *In the next two days the organism becomes rapidly* modified into a sausage-shaped larva, measuring 150 μ in length by 10 μ in *diameter. Multiplication of the nuclei of the intestinal tract proceeds* rapidly and the tail is reduced to a stump. Between the third and the seventh days the internal organization becomes more definite (Figs. 261 and 262 *A*), so that an esophagus consisting of an anterior muscular portion (*ae*) and a posterior glandular part (*pe*) become differentiated; intestine (*i*),

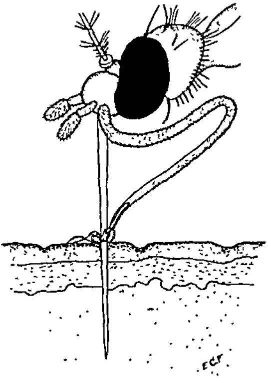


Fig. 263.—Diagram of a female mosquito discharging mature filaria larvæ while securing [illegible] The stylet apparatus, consisting of *labrum-epipharynx, hypopharynx, maxillæ* [illegible] wound. (Original.)

rectum (*r*) and anal opening (*a*) are distinct; and the digestive tract as a whole becomes separated *from the somatic layers by an intervening body* cavity. The genital primordium is still undeveloped. The larva now measures 225 to 300 μ in length by 15 to 30 μ in cross-section. Three subterminal caudal papillæ now appear.

During the beginning of the second week the second moult (*i. e.*, the moult of the first true sheath) takes place. The worm now rapidly elongates until it reaches a length of 1.4 to 1.5 mm. Active movement is resumed and the parasite migrates from the thoracic muscles into the head, where it lies coiled up (Fig. 262 *B*), ready to enter the proboscis sheath (*e. g.*, the labium). The complete period of development in the mosquito varies from ten days to six weeks or more, depending primarily on the temperature

and moisture, but also, perhaps, on the species of mosquito. When the infected mosquito prepares to take a blood meal from the next individual, following the maturity of the larvæ, they migrate down through the hemocele within the labium, and emerge through the tip of the terminal portion (the labella), near the site of the proboscis puncture (Fig. 263). According to Fülleborn (1907), who studied the subsequent behavior of the microfilariæ of *Dirofilaria immitis*, the larvæ do not enter the puncture wound but invade the superficial layers of the skin on their own behalf, a portion of the larvæ successfully penetrating through to the peripheral blood capillaries. On the other hand, Yokogawa (1938, 1939) states that actual transmission cannot occur except where there is lymph exudate from the puncture wound, to induce a lymphotactic reaction on the part of the larvæ; that mature larvæ of this species fail to penetrate unbroken skin of man or laboratory animals, and that only a limited number of those invading the puncture wound reach the subcutaneous tissues and lymph spaces.

The studies of O'Connor and Beatty (1938) indicate that some of the mature larvæ may migrate from the thoracic muscles to the mosquito's abdomen, where they are apparently locked in, unless they later return to the thorax or escape through the ruptured integument in case the mosquito is crushed while taking a blood meal from a human subject.

Hu (1935) found viable infective-stage larvæ of *W. bancrofti* in *Culex pipiens* var. *pallens* as long as seventy-nine days after exposure. Moreover, he has proven that repeated infections of the same mosquito may occur.

Mosquitoes in which complete development of *Wuchereria bancrofti* has been demonstrated to occur, from the microfilaria to the infective-stage larva in the proboscis of the mosquito, are listed in the accompanying table (Table 4).

TABLE 4.—DEMONSTRATED MOSQUITO HOSTS OF *Wuchereria Bancrofti*, WITH FULL DEVELOPMENT TO INFECTIVE-STAGE LARVÆ.

Note. (1) An asterisk (*) preceding a species name indicates particularly important hosts in Nature

(2) Where *W. bancrofti* and *W. malayi* are coëxtensive, it is entirely possible that, [illegible]

[illegible]

**Cul*[illegible] [illegible]. China, Formosa, Philippines, [illegible] [illegible]ia, India, Egypt, Tanganyika, Zanzibar, [illegible] Guiana, British Guiana, Brazil, United [illegible]

[illegible]

C. alis. Indonesia.
C. annulirostris Indonesia
C. bitæniorhynchus. Indonesia.
C erraticus. United States (experimental only)
C. erythrothorax. United States (experimental only)

[illegible] Japan, Cairo (Egypt), United States

[illegible]

C. salinarius. United States (experimental only) [illegible]
C. sinensis. Japan.
C. sitiens. Indonesia.
C. tarsalis. United States (experimental only).
C. triseriatus. United States (experimental only)
C. tritæniorhynchus subsp. Indonesia.
C. vagans. China, N. India.

TABLE 4 — DEMONSTRATED MOSQUITO HOSTS OF *Wuchereria Bancrofti*, WITH FULL DEVELOPEMENT TO INFECTIVE-STAGE LARVÆ (CONCLUDED).

Note (1) An asterisk (*) preceding a species name indicates particularly important host in Nature.

(2) Where *W bancrofti* and *W malayi* are coextensive, it is entirely possible that in the incrimination of certain species of *Anopheles* and *Mansonia* as mosquito hosts, the two species of filariæ may have been confused, *i e*, *W bancrofti* may have been designated when *W malayi* is the filaria present in the mosquito,

C vishnui. India

...les, St Croix (W. Indies),

...*Aegomyia scutellaris* auct)

A tæniorhynchus St Croix (W Indies)
A. triseriatus United States (experimental only)
A togoi Japan
A rigilax Indonesia and Australia
Mansonia annulata Indonesia

...laya, Indonesia

...perimental only)

A amictus N Queensland (experimental only)
A aquasalis Brazil
A annularis (syn *A fuliginosus*) India
A bancrofti Indonesia, Celebes
A
**A*
A
**A* ...ngo, Zanzibar
A
A hyrcanus var *sinensis* Shanghai, Japan
A koliensis S Pacific islands
A leucosphyrus var *hackeri* Kabæna Islands (Indonesia)
A maculatus Celebes
A oswaldoi Brazil (experimental only)
A pallidus India.
A
A
A
**A*
**A*
**A punctulatus punctulatus* S. New Guinea, Celebes.
A rhodesiensis Sierra Leone (experimental only)
A rossi India
A squamosus squamosus Sierra Leone.
A stephensi subsp India
A. subpictus subpictus (fresh- and brackish-water types) India
A. sundaicus India.
A triannulatus Brazil (experimental only).
A vagus vagus Indonesia
A varuna India
A. walkeri United States (experimental only)
Psorophora confinnis Puerto Rico and United States (experimental only)
P discolor. United States (experimental only)

In many other culicine and anopheline mosquitoes development is aborted or incomplete. Hu (1935) found that the immature larvæ of *W. bancrofti* in *Aëdes albopictus* and *Armigeres obturbans* may penetrate into the thoracic cavity, where they die without completing their development. Edwards states that the almost universal association of *Aëdes ægypti* with *Culex "fatigans"*, together with the diurnal feeding habits of the former species, would render it less liable to infection and less able to develop a fixed relationship with the worms than the latter species in case the larvæ have a definite nocturnal periodicity.

In addition to mosquito hosts, Raynal (1937) states that Yao, Wu and Sun obtained complete development of *Mf. bancrofti* in seventeen out of fifty-nine specimens of *Phlebotomus sergenti* var. *mongolensis*, fed on the blood of an infected patient.

Manson-Bahr found that when fewer than one microfilaria were present in 2 c.mm. of the patient's blood, the appropriate mosquito frequently failed to acquire an infection; that when there were ten or more embryos per c.mm. the infection tended to kill the mosquito, and that when fed on blood containing about three embryos per c.mm. the optimum development took place in *Aëdes "variegatus"*.

Development in the Human Host.—From the time the infective-stage larvæ of *W. bancrofti* escape from the proboscis sheath of an infected mosquito onto the skin near the site of the puncture wound until adult worms are known to be present in lymphatic vessels or lymphoid tissues, approximately one year or more is required. However, the actual route of migration of the larvæ to the foci where the adults are lodged and their development during this incubation period are as yet relatively unknown. However, the large number of patients among American troops who became infected in the South Pacific during 1942–1944 has provided considerable information of the activities of the filariæ during the biological incubation period. The filariform larvæ actively enter the skin and probably on reaching the deeper cutaneous and subcutaneous lymphatics continue to [illegible]

slowly and [illegible]

nodes in va[illegible] in the groin glands and in the glandular tissues of the scrotum, particularly around the epididymis. In these locations they reach maturity, mate and the female worms begin parturition. The male and female worms live [illegible]

[illegible] between the glands, in the glands themselves, or even in the thoracic duct.

Epidemiology.—Man is the only known definitive host of *W. bancrofti*, but many species of mosquitoes have been proven, either by natural or by experimental infection, to be suitable intermediate hosts. The mosquitoes obtain the microfilariæ from the peripheral blood of man. After development to the infective-stage in the thoracic muscles of the mosquito, the larvæ migrate down the proboscis sheath (*i. e.*, through the hemocele of the labium) and are discharged near the puncture wound in the victim's skin Yokogawa (1939) has found the infection-rate of mosquitoes (*Culex*

quinquefasciatus) extremely low in population groups of Ishigaki Island, near Formosa, where Bancroft's filariasis was fairly prevalent. He believes that the infection has difficulty in spreading because of the low parasite index in the mosquito coupled with the small chance the larvæ have of reaching the subcutaneous tissues of man and of establishing themselves in lymphatic vessels or tissues.

In highly endemic areas exposure begins early and continues throughout ... gradually builds up with each decade, although it

...

area, so that reexposure does not take place, the symptoms are likely to subside and the chronic sequelæ may not develop.

Pathogenesis, Pathology and Symptomatology.—The disease in native populations produced by *Wuchereria bancrofti* is divided into four more or less distinct stages or periods, namely (1) *the biological incubation period*, (2) *the symptomless patent period*, (3) *the acute stage*, and (4) *the chronic stage*.

The effects of *Wuchereria bancrofti* on a particular human being are ... several factors including the tolerance of the individual to

...

in the body where immature or mature filariæ become temporarily or permanently lodged, and the possibility of supervening infection with streptococci, staphylococci or pathogenic fungi. In intolerant individuals the metabolites of the inoculated larvæ tend to provoke increasing allergic manifestations as the young filariæ circulate through the lymphatic vessels. This is at first evidenced by urticaria and "fugitive swellings," with edema, vascular engorgement and perivascular infiltration with numerous eosinophils.

When living immature or adult filariæ become lodged in the smaller lymphatic vessels, including the afferent lymphatics leading into lymph nodes, the "parasites create ...
to destroy, engulf and absorb ...
lining of the vessel becomes ...
Typically fibrin is deposited on the surface ...
of the vessel becomes edematous, and if the reaction is severe there is a heavy infiltration of eosinophils. Loose aggregates of histiocytes, epithelioid cells, lymphocytes and frequently foreign-body giant cells appear and multiply by mitosis within the lumen of the vessel, then become associated by small fibrinous threads and tend to produce endolymphatic obliteration. Meanwhile perilymphatic changes of a similar type constrict the wall of the vessel and may strangulate the worm unless it is able to migrate into undamaged lymph channels. (See Fig. 264.)

When living worms become lodged in lymph nodes, the afferent lymphatic vessels become hypertrophic, with varices extending into the deeper portions of the nodes. The worms are rapidly surrounded by masses of eosinophils, edematous lymph follicles and intact centers of rapidly dividing cells. The amount of endothelial hyperplasia, initiated by reticulo-

endothelial activity, governs the progress of the lesion from that of cellular granulation to one of proliferative granulation and repair, and thus determines the degree of degeneration of the filariæ caught in a lymph node. Michael (1944) states that the "filarial granulation tissue . . . is almost pathognomonic of this disease," while Hartz (1944) regards it as characteristic but not specifically pathognomonic.

This early characteristic lesion is transformed into one having a central core of necrotic tissue surrounded by a radiating zone of proliferating endothelial cells, epithelioid cells, foreign-body giant cells and fibroblasts, and a dense peripheral infiltrate of eosinophils. Whether the tissue reaction is in a lymphatic vessel or within a lymph node in which the filariæ are trapped, the final result is essentially the same, namely the death and absorption (or calcification) of the parasite, fibrous tissue replacement of the earlier cellular infiltrate and the disappearance of the diagnostic criteria.

At times, in highly reacting patients, immature filariæ escape from blocked channels without apparent injury, only to provoke similar tissue reactions at other sites of lodgment. In mildly reacting or non-reacting individuals the growing worms migrate rather freely through lymphatic channels, until they become mature. Mating then occurs and the fertilized females discharge microfilariæ into lymphatic channels. Parturition almost invariably provokes moderate to severe local tissue reaction, even in tolerant hosts, with resultant subacute to acute manifestations of filarial lymphangitis and/or lymphadenitis. Increasing evidence supports the conclusion that these initial tissue responses are stimulated by the filariæ and their metabolic products and do not result from supervening infections with β-hemolytic streptococci, staphylococci or pathogenic fungi. Later, in the chronic stage, after fibrosis has developed, there is abundant opportunity for secondary invaders to produce a neutrophilic inflammatory reaction.

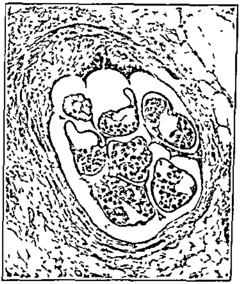
The increasing obliteration of lymphatic vessels and blockage of lymph flow result in an insidious retrograde extension of the lesion and fibrous tissue repair. This is responsible for the development of the chronic sequelæ, such as lymph varix, varicose groin gland and elephantiasis.

The Incubation Period.—This covers the time from exposure, when the infective, third-stage larvæ escape onto the skin from the proboscis of the mosquito, until microfilariæ are first discharged from the mother worms and appear in the circulating blood. About one year is required for the larvæ to migrate to the lymphatic tracts or lymphoid tissues and to mature. Essentially nothing is known concerning the sequence of events or the morphological changes that occur in the worms. The tissue changes in the patient's body may be inconsiderable. On the other hand, there may be acute inflammatory reaction wherever immature worms become temporarily or permanently lodged in lymph nodes, with lymphadenitis at, and retrograde to, the site of obstruction. In the South Pacific islands this [illegible]

discharged daily by the mother worms (according to Lane, who is supported by the evidence of O'Connor, about midday in the periodic type of the

organism). In so far as is known there is no essential tissue reaction or cellular infiltration in the vicinity of the living parent worms or their progeny. Even the death of the microfilariæ produces no marked local or systemic pathology, and there is typically no significant eosinophilia. However, it is probable that some local tissue alterations do occur around the adult worms after a period of time

The Acute Stage.—In many patients who harbor *Wuchereria bancrofti*, possibly the majority, O'Connor (1932) has found that the living adult worms residing in compact tissues produce dilatation of the lymphatic vessels, and those in lymph channels in connective tissue at times cause a marked hypertrophy of the surrounding tissues (Fig 265). Some lymph



tion by Dr F W O'Connor, courtesy of United States Army Medical Museum)

Fig 265 —Section through a lymph node with gravid female of *Wuchereria bancrofti* encapsulated in a pocket of fibro-connective tissue × 66 (Original photomicrograph from a preparation by Mr Conrad Bauer)

stasis may be occasioned but without inflammatory reaction Little by

giant cells, eosinophils, large mononuclears and finally fibroblasts, produces an encapsulation of the dead or dying worms. As the worms undergo

h are believed

, as well as for

d Rao, 1930).

Not uncommonly this period is ushered in by *prodromal symptoms* of

toxic malaise, mental depression, and by frontal headache, or by urticarial rash. There usually follows an acute *lymphangitis*, accompanied by "*filarial fever*." The lesion, which is usually on the lower extremity, is linear, elevated, hyperemic and excruciatingly painful to the touch. In a few days these manifestations subside, but tend to recur periodically, in women at times with the menses, in men usually less frequently. Gradually these attacks become less severe and the involved lymph channels less painful at the time of the attack.

The Chronic Stage.—This develops gradually and is accompanied by *lymphocele* and *lymphvarix*, frequently with rupture, in the less fibrosed variety, or by enlargement of the involved member or organ (*elephantoid type*).

FIG. 266.—Section of an encapsulated calcified female *W. bancrofti*, × 80. (Photomicrograph from a preparation by Dr. F. W. O'Connor, courtesy of United States Army Medical Museum.)

Clinical filariasis bancrofti among American troops in the South Pacific, with especially heavy first exposure in a relatively large group of highly susceptible young adult males, has provided an unusual opportunity to study the early manifestations of the disease. In his report on the findings in 268 cases, King (1944) found that the period between earliest exposure and the development of symptoms varied from three to sixteen months; that the onset was accompanied by pain and swelling or redness of the arm, leg or scrotal area, but that heachache and fever were uncommon (about 20 per cent of cases had fever of a mild type and of short duration); that the cardinal manifestations were lymphangitis, usually with an associated lymphadenitis, frequently or eventually an acute inflammation of the scrotum and its contents, and that relapses of the acute syndrome were frequent. The lymphangitis in 51 per cent of the patients was in an upper extremity, with red streaks, patches, or subcutaneous edema and overlying

redness. The lymphadenitis was most commonly epitrochlear. The genital involvement consisted for the most part (71.6 per cent) of inflammation *of the spermatic cord, epididymis, testis or entire scrotum, at times* accompanied by exquisite pain. In a study of white immigrants in Samoa, who had been less heavily exposed than the American troops but repeatedly over a period of many years, Webster (1946) found that 50 per cent of the males and 40 per cent of the females had symptoms of filariasis. Many of these had yearly bouts of lymphangitis and fever. Elephantiasis, slight to severe, was not present before the forty-first year and increased in severity with age. In a survey of 5000 natives in the Belem endemic area of Brazil, Causey, Deane, da Costa and Deane (1945) found microfilariæ only in 535, elephantiasis only in 58, both types of evidence in 6, with a total of one or the other, or both in 599, or 12 per cent.

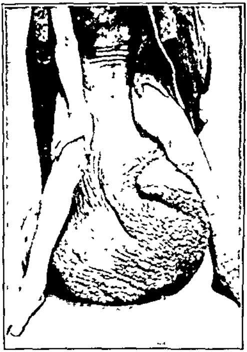


FIG. 267.—Elephantiasis of the scrotum in filariasis bancrofti, in a Japanese subject (From 'Medicina Bildaro Fotografa,' Elefantiazo kaj Filariazo.)

Probably the commonest effect of *Wuchereria bancrofti* in the lymphatics is mechanical obstruction of lymph flow, giving rise to varix lymphaticus. In case of blockage of the thoracic duct, the lymphatics of the abdomen, pelvis, groin or scrotum may be enormously distended by chyle, forced to find collateral tracts in order to enter the general circulation. If the integument of the scrotum is involved, "lymph scrotum" results; if the groin is involved, "varicose groin-glands" develop, if the lymphatics of the bladder or kidneys are affected and the tension becomes too great, rupture of the vessels results in chyluria. Similar distention and rupture in the tunica vaginalis may give rise to "chylocele," and of the peritoneum, to chylous

ascites. Similar obstructions of other parts of the lymphatics occasion comparable pictures. In such cases microfilariæ can usually be demonstrated in the blood as well as in the chylous fluid.

In a large proportion of ca...

... around the lymph tracts and glands. In 95% of the cases the parts affected are in the lower extremities and the scrotum (Fig. 267). In women the vulva commonly and mammary glands rarely are the seat of enlargement.

Knott (1938) states that elephantiasis is not necessarily a steadily progressive disease. Usually the swelling appears in childhood or during adolescence and progresses for five or ten years, then becomes stationary. ... ...tly further enlargements, mostly with ... with cardio-renal dysfunction. In the early stage involving the lower extremities only the skin between the ankle and knee is affected: it first manifests a firm springiness, then a tumor-like hardness, with crusts, warts, nodules, etc., due to improper desquamation of the horny layer. It becom...

The elephantoid tissue usually consists of lymph and adipose tissue in a hard matrix of fibrous material, covered by a tightly stretched, thickened skin, almost completely deprived of normal blood flow, readily cracking and easily invaded by pyogenic bacteria or pathogenic fungi. On pressure a non-pitting edema is demonstrated.

At times adult and immature *W. bancrofti* have been recovered from rather unique foci. Wright (1934) and Fernando (1935) each removed an adult filaria, believed to be *W. bancrofti*, from the anterior chamber of the eye of a Hindu student suffering from a transient iritis and having microfilariæ in his circulating blood. It is possible, however, that these immature worms may be *Dirofilaria conjunctivæ*. (*Vide infra.*)

Although it is not usual for the microfilariæ to produce damage to the tissues sufficient to provoke symptoms, it is conceivable that they may ... ...iose of the brain, and cause acute ... Popon and Prjadko (1926) demon- ... ...al encapsulation following introduc- ... ...ported right hemiplegia in a patient

... *Produced by Secondary Invaders.*—A considerable number of cases of lymph varix and elephantiasis manifest symptoms of lymphangitis of the various parts of the lymphatics. (See Fig. 268.) The condition may be localized or may become generalized. It is usually attended with "elephantoid fever," a pyrexia of recurrent type, with rigor and terminal diaphoresis, commonly confused with malarial fever. Dermatitis and cellulitis may develop, particularly in the elephantoid tissues. Workers in British Guiana have demonstrated the presence of staphylococci or streptococci in cases with inflammatory complications of the lymphatics. Anderson (1924) believed that the damage produced

by the filaria worms in the intima of the vessels prepares the way for invasion of the bacteria, which may have been responsible for the changes produced long after the adult worms have died and the microfilariæ have disappeared from the circulation, while Grace and Grace (1931) strongly support the view that lymphangitis in filaria-infected persons invariably results from hypersensitivity to certain strains of hemolytic streptococci. Drinker (1936) has demonstrated that the loss of normal lymphatic circulation predisposes to streptococci infection, with manifestations of severe chill and high fever. However, McKinley (1931), Michael (1944) *and Hartz (1944) have found no evidence of bacteria in the actual focal* centers of the inflammatory reactions around immature or mature filariæ. Furthermore, Iyengar (1939) has found from his extensive epidemiological studies in India that there is a significant correlation between the parasite rate (*i. e.*, percentage of patients with microfilariæ in their circulating blood at night) and filarial disease (for 216 localities $r = +0.7644$). More recent bacteriological and clinical studies in Puerto Rico and elsewhere have indicated that the beta-hemolytic Streptococcus is frequently present in chronic infections with *W. bancrofti* and that the activity of this organism is correlated with recurrent lymphangitis In many instances where culture technics have been negative specific serological methods have demonstrated the presence of the bacterium. Thus, it would appear that in many instances previously denied the beta-hemolytic Streptococcus may play some part in the development of the chronic filarial lesion and particularly in the reactivation of the inflammatory process around the parent worms. Yet, as Coggeshall (1948) has pointed out, the lymphangitis in Bancroft's filariasis is not identical with that observed in streptococcus infections not complicating filariasis and fails to respond to chemotherapeutics or antibiotics which specifically effect streptococcus.

Lymph Varix and Elephantiasis of Non-filarial Origin.—These diseased conditions, without inflammatory complications, occur in certain areas where *Wuchereria bancrofti* is not known to occur, and under such circumstances must be attributed to a lymph stasis produced by an unknown cause. Where lymphangitis is an accompaniment, it is probably of secondary septic origin. Even in endemic foci of Bancroft's filaria about 5 per cent of tropical elephantiasis is estimated to be of uncomplicated bacterial origin (Suarez, 1933).

Diagnosis.—A history of one or more episodes of lymphangitis, lymphadenitis, or acute inflammation of the scrotum and its contents (especially the epididymitis), the vulvæ or mammary glands, together with residence in an endemic area, suggests the possibility of Bancroft's filariasis, but many other causes must be ruled out, including other types of filariasis, such as infection with *Wuchereria malayi*, *Loa loa*, *Onchocerca volvulus*, *Acanthocheilonema streptocerca*, etc. (*Vide infra.*)

Infection with *Wuchereria bancrofti* can be demonstrated in a proportion of infected individuals by the recovery of the microfilariæ of this organism from blood films or from chyl
percentage of positive findings
cases than in late cases, due to
charged into the circulation after the lymph flow becomes obstructed or the

mother worms become moribund. In some patients, however, health[illegible] parent worms, in foci as yet unaltered [illegible] microfilariæ. It must be remembered, [illegible] not be found during the biological *incubation* period and that they may not reach the circulating blood, even *though* the female worms mature and become parturient.

In regions where the organism manifests nocturnal periodicity, blood for examination should be obtained between 10 P.M. and 2 A.M. For the non-periodic type of the South Pacific islands the microfilariæ are present in peripheral blood both diurnally and nocturnally. For routine examination, thick blood-films are preferred. About 10 cmm. of blood are placed on an absolutely clean slide, covering an area about 1.5 cm. in diameter. The

FIG. 268.—Elephantiasis in a Hindu girl in British Guiana; filariasis bancrofti with probable septic complications (After Sambon, Journal of Tropical Medicine and Hygiene.)

film is dried thoroughly, and is either dehemoglobinized and stained by the Giemsa technic or by hematoxylin methods. Knotts' technic consists in adding 10 cc. of formalin to 2 cc. of blood drawn from the patient, centrifugalizing the material at about 2000 r.p.m. for five minutes and examination of the stained sediment for microfilariæ. (See Chap. XXXIII, pp. 575-577.) In patients, with pathological members or organs, suspected to have been caused by *W. bancrofti* but without microfilariæ in the blood,

x-ray films of the affected part may demonstrate multiple, pinpoint sites of calcification in the centers of fibrosed tissue. This picture is pathognomonic of the disease in its chronic stage (O'Connor, Golden and Auchincloss, 1930).

The microfilariæ of *W. bancrofti* must be distinguished from those of other filaria worms of man, particularly *W. malayi*, which also is found in patients with elephantiasis.

The use of 0.025 to 0.25 cc. of a 0.1 per cent sterile solution of pulverized antigen, introduced intradermally produces an immediate positive skin reaction in about 90 per cent of *W. bancrofti* patients (Taliaferro and Hoffman, 1930; Fairley, 1931). More recently Bozicevich and Hutter (1944), as well as other workers, have demonstrated that antigen, prepared from adult *Dirofilaria immitis* by physiological saline extraction, in a 1:8000 dilution, provides 90 to 100 per cent positive intradermal reactions in early cases of *Wuchereria bancrofti* (*i. e.*, during the biological incubation period) and gives no false positives in this dilution. Franks and Stoll (1945) and Warren, Warren and Hunter (1946) have isolated the microfilariæ of *D. immitis* from dog's blood for preparation of antigen. It must be borne in mind, however, that this filaria-group reaction does not eliminate the possibility of infection with some other filaria worm in areas, as in Africa, where two or more types of human filariasis are coextensive. Moreover, Augustine and l'Herisson (1946) have suggested, on the basis of comparative studies of antigen prepared from *D. immitis*, *Setaria equina* from the horse, *Litomosoides carinii* from the cotton rat and *Vagrifilaria columbigallinae* from the ground dove, that positive skin reactions in man may possibly result from sensitization following introduction and destruction of microfilariæ other than those of *W. bancrofti*, as in "bites" of infected insects. (For technic of preparation of the antigens, *vide* pp. 601–609.)

Therapeusis.—(1) *Specific Chemotherapy.*—In recent years several groups of investigators have explored the filaricidal properties of many drugs, utilizing dogs infected with *Dirofilaria immitis*, cotton rats parasitized with *Litomosoides carinii* and clinical material. Several trivalent and pentavalent antimonials and arsenicals, phenyl arsenoxides (Otto and Maren, 1947), cyanine dyes (Welch *et al.*, 1947) and Hetrazan (1-diethyl carbamyl-4-methyl piperazine HCl) have been given particularly critical trial. Even though a drug may be highly efficacious in destroying filariæ in laboratory animals, it is not *ipso facto* satisfactory in human filariasis. Culbertson, Rose, Hernández Morales, Olivér González and Pratt (1946) have concluded that of the well tolerated drugs neostibosan gives the most satisfactory results. This pentavalent antimonial is prepared freshly as a 5 per cent solution and is administered daily by vein in 2.5 to 10 cc. amounts until 5 to 6 Gm. have been employed for a person weighing 50 to 60 Kg. Although the cyanine compounds are specific against *Litomosoides carinii*, similar filaricidal action has not been demonstrated in Bancroft's filariasis. Hetrazan (Santiago-Stevenson, Olivér González and Hewitt, 1947) appears to act rapidly on inhibiting microfilarial production and death of the parent worms, but sudden death of the worms conceivably produced hypersensitivity to their metabolites, with severe allergic

manifestations. In a clinical study of 239 cases of Bancroft's filariasis in British Guiana (118 asymptomatic with microfilariae in their circulating blood, and 121 symptomatic and all but 17 with microfilariae) Kenney and Hewitt (1949) administered [illegible]
of 0.2 to 2.0 mgm. each per kilo [illegible]
with only mild reactions, apparently all due to filarial sensitization and not to the drug. In doses of 0.5 to 2.0 mgm. per kilo three times daily the microfilariae usually disappeared within one week and the blood films usually remained negative. In the symtomatic cases, even including those [illegible]

of the filariae. These workers conclude that asymptomatic as well as symptomatic cases should be given the benefit of Hetrazan therapy, since cumulative evidence indicates that it kills adult worms as well as microfilariae. Because of the ease of administration of Hetrazan and the relatively mild reactions experienced, this drug appears to be the first really satisfactory chemotherapeutic for treatment of infections with *Wuchereria bancrofti*.

(2) *Surgery.*—Various operative procedures have been advocated. In some cases obstruction of lymph flow may be removed and elephantoid tissue wholly or partially excised, as, for example, by a modified Kondolean operation (Auchincloss, 1930). In other instances deep lymph drainage has been practiced.

Knott (1938) has had excellent results with pressure bandaging of elephantoid legs. He wraps the member tightly with six-inch strips of bath towelling, which he fastens with dextrin syrup, and covers this with cotton elastic crepe bandage and an outer muslin bandage to keep out dirt. Walking is required to prevent cyanosis of the leg and to reduce the lymphedema. As the skin shrinks, new, smaller bandages are applied. When the member is sufficiently reduced, an elastic stocking may be used. In early or mild cases complete return to normal size has been effected, normal skin texture has been obtained and the febrile attacks have been eliminated. In advanced stages the lymphedema and hyperkeratosis are reduced but the underlying fibrosis is not appreciably decreased. The bandage serves to increase the fluid pressure in the leg, so that the lymph does not stagnate but is carried up to normal channels. The bandage is not removed for any length of time except when infective inflammation of the skin develops.

Golden and O'Connor (1934) found that *x*-ray therapy is not particularly helpful. Jaffe (1945) states that irradiation is neither harmful nor helpful in influencing the frequency and severity of recurrent attacks of lymphangitis and lymphadenitis, or the size or tenderness of enlarged glands.

In septic complications sulfonamides, penicillin or streptomycin therapy may be indicated.

Lane (1948) sums up his views regarding therapeutic relief in Bancroft's filariasis as follows: (1) Chemotherapy by vein, even in adequate concentration, "has little prospect of success," (2) chemotherapeutics introduced

into selected locations in the lymph stream seem more promising; (3) x-rays have sterilized and killed worms in selected sites, but their application must be less damaging than the infection itself; (4) "there is little hope of complete un-worming by surgical excisions," because of the multiplicity of foci where the worms become trapped, yet "surgery will right inconvenience, or will remove a focal spot."

Prognosis.—In subclinical or "symptomless" cases the outlook is fair, although reexposure to filarial or pyogenic infection, or the gradual development of the lesions to a clinical grade may be anticipated. In clinical cases, even with surgical intervention, the prognosis for recovery is poor, although the patients may live for many years. With Hertrazan therapy death of the parent worms as well as the microfilariae appears to be demonstrated. Clinical improvement following Hertrazan treatment, even in advanced cases, appreciably improves the prognosis.

Control.—Until the development of the newer insecticides no satisfactory method had been devised for the reduction or eradication of Bancroft's filariasis from a heavily endemic area However, measures directed against malaria mosquitoes in the Southeastern United States and yellow-fever mosquitoes in Bahia State, Brazil apparently reduced contact of house mosquitoes with *W bancrofti* cases in the former Charleston, South Carolina area of filarial endemicity below the threshold of transmission and greatly reduced the transmission in Bahia State.

With the introduction of DDT prophylaxis in malaria control, the spraying of homes to kill adult mosquitoes and of the breeding places to kill the larvae has become practical These technics are particularly applicable to the destruction of all mosquitoes which transmit *W. bancrofti* with the possible exception of species of *Mansonia*. In any control program directed against Bancroft's filariasis, it is first necessary to determine the mosquitoes responsible for transmission and then learn where they breed, usually nearby human habitations DDT should be employed in spraying the homes and as a larvicide

There is some evidence that therapeutic prophylaxis is of practical value.

Wuchereria malayi (Brug, 1927) Rao and Maplestone, 1940. (The Malayan filaria, producing Malayan filariasis)

Synonyms —*Filaria malayi* Brug, 1927; *Microfilaria malayi* (Brug, 1927).

Historical and Geographical Data.—This microfilaria was first obtained by Lichtenstein from natives of Celebes, and was studied by Brug (1927), who found it to differ from the common microfilaria (*Mf. bancrofti*) and designated it *Filaria malayi*. The discovery and description of the adult worms by Rao and Maplestone (1940) in India confirmed Brug's study of the microfilaria in distinguishing it as a separate species, but generically related to *W bancrofti*. In so far as has been determined, man is the only definitive host of this parasite.

Wuchereria malayi has a rather extensive distribution in Indonesia (Brug and DeRook, 1933), Borneo, Celebes, Ceram, New Guinea, Ceylon, Travancore, Orissa State and Centra
China, and in the region of Huchow,
Hankow, China It has also been foun

residing in the New Hebrides (Perry, 1944), and in Koreans on Oahu, Hawaii (Nelson, Webb, Bayliss and Starkey (1946). In some of these areas it is the only human filaria; in others it is co-extensive with *W. bancrofti*. In Sumatra 18 per cent of an estate population were found infected and 80 per cent of these had elephantiasis.

Morphology, Biology and Life Cycle.—In general, the adult *W. malayi* bears considerable resemblance to *W. bancrofti*. (*Vide supra.*) The worms studied by Rao and Maplestone (1940), obtained from a patient from North Travancore, India, consisted of both males and females, as were those obtained by Bonne, Lie Kian Joe, Molenkamp and Myeren (1941) from Indonesia. They are delicate, thread-like, whitish nematodes, which live coiled up in pairs (male and female) in dilated lymphatic vessels. The tapering anterior end is free of labia but is provided with two encircling rows of minute papillæ. The males measure 22 to 23 mm. in length by 88 microns in greatest diameter. The caudal extremity has about three complete revolutions and the cloacal opening lies about 0.1 to 0.14 mm.

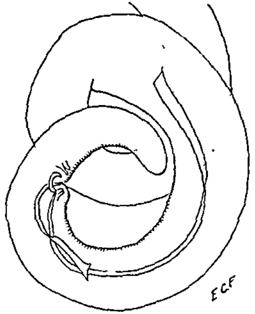


FIG. 269—Caudal end of male *Wuchereria malayi*, showing unequal copulatory spicules, curved gubernaculum, cloacal opening and the two pairs of pre- and post-cloacal papillae. (Adapted from Rao and Maplestone, in Craig and Fausts' Clinical Parasitology)

from the caudal tip. One pair of long papillæ are immediately in front and one pair immediately behind the cloaca (Fig. 269). Nearby are two pairs of smaller papillæ. The copulatory spicules differ in length and morphology. The longer measures 0.34 to 0.36 mm., the shorter, 0.11 to 0.12 mm. Guarding the opening of the sex canal is a small naviculate gubernaculum. The single complete female studied by Rao and Maplestone [illegible]

The microfilariae of *W. malayi* (Fig. 270) measure [illegible] which by 5 to 6 μ in greatest diameter. They are invested with a sheath, which

is very much longe ula is very delicately striated. and bears a double stylet proces _ 12 to 16 μ. The excretory pore is 30.09 per cent distant from the anterior extremity, the large excretory cell, 37.07 per cent, the G_1-cell, 69.33 per cent, and the anal pore, 82.28 per cent. From the region of the anal pore the body decreases to an acuminate caudal extremity. The extreme caudal termination is swollen to accommodate an elongate nucleus, while about 10 μ in front of this nucleus there is an oval nucleus, the two being much more darkly stained than the other nuclei of the microfilaria. The living microfilaria is stiff, with secondary kinks, thus resembling *Mf. loa*, rather than *Mf. bancrofti*, in its movements. (See Table 3, p. 504, for comparison of these three species of microfilariæ.) *Mf malayi* exhibits a partial nocturnal

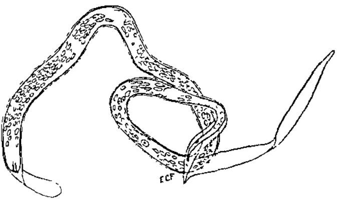


FIG 270 — Microfilaria of *Wuchereria malayi* For explanation see Fig 260 × 666. (Original from a blood-film from Celebes, obtained by Brug)

periodicity: Yen and Chang (1935) found the embryos in peripheral blood of patients between 4 P.M and 2 P.M. the next day, with a maximum surge at 4 A.M.

In the mosquito host the microfilaria migrates from the stomach to the thoracic muscles, where Feng (1936) has found that it develops through three true larval stages, with two ecdyses, before it becomes mature and migrates down through the hemocele in the labium, to be deposited on the victim's skin at the site where the mosquito takes its blood meal. Feng (*l c*) has also demonstrated that the cephalic space of the microfilaria forms the buccal cavity of the mature larva, that the anterior nuclei form the esophagus, the middle nuclei the mid-gut, and that the "G-cells" of the embryo are not genital primordia but are the cells from which the rectum and anus of the larva are formed.

Epidemiology.—Infection is transmitted to man by certain species of mosquitoes which deposit infective-stage larvæ on the skin when preparing to take a blood meal. Man is the only known definitive host of the infection.

The mosquitoes which have been demonstrated to be natural intermediate hosts of *Mf. malayi* include: *Mansonia annulata*, *M. annulifera*,

M. indiana, *M. uniformis*, *M. longipalpis*, *M. indica* ... *stris barbirostris* ... 942) ... ater ... infection.

Clinical Data.—The lesions produced by the parent worms and the tissue changes developing around them have not been carefully studied. The infection is frequently associated with elephantiasis, primarily of the upper extremities, for which blockage of lymph vessels in the immediate vicinity of the adult worms is probably responsible. In North Ceram Brug (1933) found a positive correlation of 0.74 ± 0.08 between this infection and elephantiasis. In one Central ... da) Rao (1945) found *W. malayi* infectio ... There were 80 cases of elephantiasis, all involving hands or legs and none the genitalia or groin. There has been no specific therapeutic study of this infection.

Control.—Sweet and Pillai (1937), working in Travancore, India, where *Mansonia annulifera* is the chief vector of this filaria, very greatly reduced exposure to infection (as tested in children up to two years of age) by removing the water plant *Pistia stratioides*, with which the larval stages of this mosquito are associated. The breeding places of the mosquitoes as well as human habitations in endemic foci should be treated with DDT to kill the transmitters and thus break the cycle.

Genus Onchocerca Diesing, 1841

(genus from ὄγκος, hook, and κέρκος, tail)

Onchocerca volvulus (Leuckart, 1893) Railliet and Henry, 1910 (The convoluted filaria, producing onchocercosis, onchocerciasis or "coastal erysipelas.")

Synonyms.—*Filaria volvulus* Leuckart, 1893, *Microfilaria nuda* Rodenwaldt 1914; *Onchocerca cæcutiens* Brumpt, 1919

Historical and Geographical Data.—This worm was first described by Leuckart (1893) from specimens obtained from a native of the Gold Coast, West Africa. On the Pacific slope of Guatemala Robles (1915) found an *Onchocerca*, which Brumpt bel ... graphical ar ... (1923) repo ... study most ... to the same ... *Simulium damnosum*, was the intermediate host of this filaria in Africa. The infection has been found to be relatively common along the West Coast of Africa from Sierra Leone to the Congo basin. The incidence is particularly high in the Belgian Congo, where 68 per cent of the natives in some areas are parasitized. Other important endemic foci in Africa are the Gold Coast, Liberia, French Equatorial Africa, the French Congo, the French Sudan, western Anglo-Egyptian Sudan (Bahr-el-Ghazal Province; Kirk, 1947), eastern Tanganyika (39 per cent of 1763 hospital outpatients infected according to Gabathuler and Gabathuler, 1947), Senegal, Nigeria, Ugand ... it is confined to certain ... of the Continental Divid ... southern states of Mexic ...

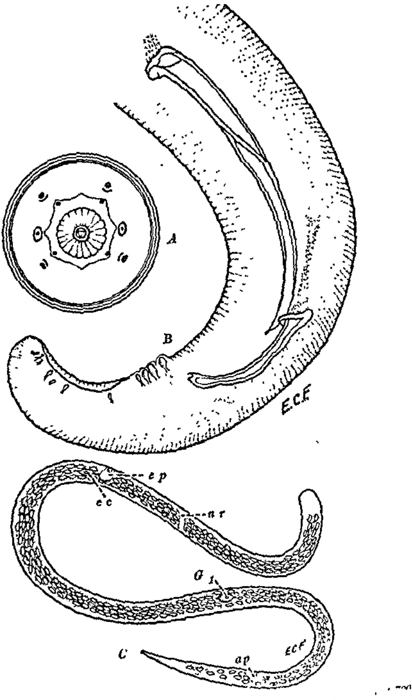
the development of information concerning the problem of onchocercosis in Mexico the reader is referred to "Datos Historicos de la Onchocercosis en Mexico a Traves de la Literatura Respectiva" by Benitez Soto, published in Rev Mex Cir, Gin. y Cáncer, *14*(6), 171–192, 1946. There is no extant evidence that the Guatemalan and Mexican disease was brought to the Americas by infected Negro slaves The infected areas are primarily inhabited by Amerinds who have within recent decades had little, if any, contact with Africans Nevertheless, it is believed that in the early colonial days, when Negroes were employed for heavy labor throughout Mexico and Central America, the infection became established in suitable localities and was perpetuated in the native population Stoll's (1947) estimate of the world incidence of onchocercosis is 19 8 millions, of which 19 millions are allocated to Africa and 800,000 to Guatemala and Mexico This latter figure is undoubtedly much higher than fairly accurate surveys can justify

Structure and Life Cycle of the Worm.—The adult worms live typically in tumors in the subcutaneous or connective tissues. When alive, they are white, opalescent, fairly transparent nematodes, with conspicuous transverse annular thickenings of the cuticle. The body is filiform and narrowed at both extremities, which are bluntly rounded At the anterior extremity there are 8 small, submedian, sessile papillæ, arranged in two circlets, and a pair of large, oval, lateral papillæ (Fig 271 *A*) They are usually intimately coiled and twisted throughout the inner substance of the encapsulating host's tissues At least one male and one female reside in each nodule. The tumors range in size superficially from a filbert to a small orange, but the actual capsule is considerably smaller They may appear on any part of the body, but are most common at the junction of the long bones (African variety) and in the temporal or occipital regions of the scalp (American variety)

The males attain a length of 19 to 42 mm and have a diameter of 130 to 210 μ. The caudal extremity is curved ventrad about 720 degrees. There are no caudal alæ. There are usually 3 or 4 pairs of conspicuous, sessile, perianal papillæ (Fig 271 *B*), and several pairs of minute papillæ at the caudal extremity, but the number of these papillæ is very variable and the distribution frequently asymmetrical The two copulatory spicules are unequal in length (88 μ and 172 μ respectively) and different in structure

The females have a length measurement of 33 5 to 50 cm., and a transverse diameter of about 270 to 400 μ. The vulva lies in the plane slightly posterior to the esophagus (about 850 μ from the cephalic end of the worm) The vagina is directed backwards The uterus is typically bicornuate The embryos *in utero* are coiled on themselves and are surrounded by a thin ovoidal egg membrane, measuring 46 to 61 μ in length by 33 to 51 μ in breadth. According to Fulleborn, they have membranous polar extensions, but Blacklock (1926) makes no mention of these structures. The embryos still coiled in the egg membrane measure 264 to 290 μ by 7 to 9 μ. The microfilariæ, on escaping from the membrane, consist of two types, a large form measuring 285 to 368 μ by 6 to 9 μ and a small form measuring 150 to 287 μ by 5 to 7 μ. It seems possible that these are respectively female and male Both types (Fig 271 *C*) have a clear, nuclei-free, anterior end. In addition, the region of the excretory bladder may be seen as a nuclei-free area about one-fifth the body length from the anterior end.

The studies of Blacklock (1926) in Sierra Leone have shown that the buffalo gnat, *Simulium damnosum*, is the intermediate host. In the thoracic muscles, and possibly also the Malpighian tubules, of this gnat the microfilaria undergoes a metamorphosis, with three larval stages and two ecdyses, after which the mature, filiform larva migrates into the head and emerges through the mouth parts from the region of the labella, thus enabling it to infect another human being when the fly secures the next blood meal.



Sandground, in Strong, 1934; C, original, labelling as in FIG 200.)

This work has been confirmed in Africa (Liberia) by Bequaert (1928), in Guatemala by Strong (1931, 1934) and in Mexico by Hoffmann (1930) and other investigators. Since the microfilariæ are present in the patient's tissues but have never been found in peripheral blood, it seems likely that the gnat must not only suck blood but tissue fluids as well The time for metamorphosis within the fly requires six days or more. In addition to *Simulium damnosum*, *S neavei*, a frequent human biter in Uganda, Kenya Colony, the Belgian Congo and Nyasaland, is apparently a transmitter. In Guatemala and Southern Mexico *S. metallicum* (syn., *S. avidum*), *S. callidum* (syn., *S mooseri*) and *S. ochraceum* are likely transmitters. Although other blood-sucking flies have thus far proven resistant to experimental infection with *O. volvulus*, in the Federated Malay States Buckley (1938) has apparently found four species of *Culicoides* to be suitable intermediate hosts for the cattle *Onchocerca*, *O. gibsoni*. Several closely related but different species of *Onchocerca* which parasitize domestic and wild mammals have been reported from the endemic areas of human onchocercosis in Africa and America (Caballero, 1945).

The incubation period in the human host is one year or less. Nodules on the skin have occasionally appeared within four months after exposure to infection. Man is apparently the only definitive host of this filaria.

Epidemiology.—Although there are many unexplained factors in the epidemiology of human onchocerciasis, it is now clear that infection is acquired only in certain areas where the human population is exposed to innumerable bites of suitable species of *Simulium*, and that these blood-sucking gnats have previously become infected after removing the micro-filariæ of *O. volvulus* from the skin of infected human beings. In all known endemic areas *Simulium* breeds in fast-flowing water at several hundred meters altitude above sea-level. The larvæ and pupæ of this fly are found under stones washed by the stream, thus providing a considerable amount

(1945) and Wanson, Henrard and

nd that the transmitting agent in

45 miles distant from the breeding sites, but that the fisher folk near the breeding grounds are practically 100 per cent parasitized, while 5 miles away the incidence is 65 per cent.

Although more prevalent in adult males than in females of the same age group, the lesions are relatively common in children. Whites are much less frequently infected than natives. This is probably explained by the preference of the gnats to take blood meals in bright sunlight, so that native laborers are more commonly exposed to infection than are white overseers.

Pathogenesis, Pathology and Symptomatology.—In certain infected areas a large proportion of the human population harbors *Onchocerca volvulus*. There may be only a single nodule or several dozen may be present, either in the same stage of development or comprising old and new sites of mature and maturing worms. In approximately 95 per cent of infected individuals the presence of the adult or maturing worms in the skin provokes a fibrous, nodular encapsulation around them. In Africa, according to Strong (1934), 95 per cent of the tumors are located elsewhere than on the head, as on the chest, lower trunk or in relation to joints, even when many nodules have developed on the same patient. These nodules vary from

soft, barely palpable, to irregularly indurated masses, and are found most conspicuously developed in association with the joints, particularly those of the elbows (Fig. 272) and knees. They may *simulate juxta-articular* nodules. Their relationship to "craw-craw" and lichenification of the skin has not been definitely established. On the other hand, in Guatemala and *in Southern Mexico, the great majority of the tumors are on the scalp* (Fig. 273). The reasons for this difference in topographic distribution are not apparent, particularly since Strong (1938) was "unable to find any convincing evidence that the point at which the fly bites has any relation to the location of the tumor."

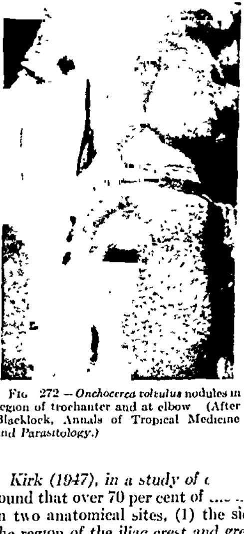


FIG. 272 — *Onchocerca volvulus* nodules in region of trochanter and at elbow (After Blacklock, Annals of Tropical Medicine and Parasitology.)

FIG. 273 — *Onchocerca volvulus* tumors on scalp of Central American child. (After R. P. Strong, in Onchocerciasis, 1934, courtesy of Harvard University Press.)

Kirk (1947), in a study of ... found that over 70 per cent of ... in two anatomical sites, (1) the sides of the chest over the ribs ... the region of the *iliac crest and great trochanters.* Puig Solanes, Vargas, Mazzotti, Guevara Rojas and Noble (1948), in a survey of this disease in southern Mexico, cite Ruiz Reyes' data ... the percentage locations for 1917 nodules, as follows: head, 37.6 (divi... 30.9, temporal, 16.6, retroauricular, 11.6 a... costal, 12.35; sacrococcyx, 11.0; trocanter, 4.8; nucal, ... 2.45 and lumbar region, 1.86. Of 5092 nodules for which data are available from the American endemic zones, 73.5 per cent were subcutaneous, 16 per cent cutaneous, 9.2 per cent intramuscular, 1.2 per cent subaponeurotic,

one was submucosal and none were intracraneal or visceral. Kirk (*l. c.*) states that the nodules are often not visible on inspection but are discovered only on palpation.

The *Onchocerca* lesion is typically a non-abscessing, fibrous tumor, which develops as an insulation around the worms, even before they have become sexually mature, and is usually fully formed in less than one year's time after inoculation. Rarely, as a result of bacterial invasion, suppuration of the nodule occurs. The tumors measure 1 to 25 mm. or more in diameter, and when excised from beneath the skin look like white, usually smoothly rounded, ovoidal or at times irregularly contoured pebbles. They are hard on palpation but are softer, cavernous and frequently yellowish internally, and usually have at least one pair of worms inextricably entangled in the fibrous matrix. The free fluid has a purée consistency and contains many microfilariæ (Fig 271C).

The nodules are clinically benign, although they may be very painful. In Africa there is characteristically an associated keloid formation. Although *Onchocerca volvulus* tumors have never been found in the deeper layers of the body, there is a suspicion that they may be attached to the inner aspect of the ribs or vertebræ in those patients in whom there are no visible or palpable nodules but in whose skin the microfilariæ may be demonstrated.

Cutaneous Manifestations.—Although the skin in onchocercosis may be dry, roughened, shiny and thickened, Goldman and Ortiz (1946) list the following varieties of dermatitis due to this cause: (1) *Licheniform*, with thickened, hyperpigmented skin and an associated intense pruritus; (2) *pigmentation dermatitis*, usually smooth, bluish-red or purplish, at times with local edema, frequently pruritic, and (3) *eczematoid*, with papulovesicular, excoriated lesions, at times impetigous, or papillomatous, verrucous and hyperkeratotic. To this classification should be added a fourth, namely *dermatographic*. Moreover, Rodham (1943) has called attention to the occurrence of adenolymphocele and scrotal elephantiasis which may result from *Onchocerca* infection.

Ocular Manifestations.—Ocular lesions and complications of the face, scalp and ear-lobes have been known to result from *Onchocerca* infection in Guatemala since the original observations of Robles (1915), Calderon (1917) and Luna (1918). More recently pathology of the eye has been found to be fairly common in Mexican patients (Larumbe, 1928; Silva, 1932). At least 5 per cent of the infected individuals in Guatemala and Southern Mexico exhibit either diminished vision or blindness in one or both eyes In Africa the associated eye defects were at first believed to be rare, but Hissette (1931, 1932, 1938) and Applemans (1935) have found these complications to be both common and serious.

Pathology of the eye in onchocercosis is more frequent in males than in females, but there is no significance with respect to the age of the patient, the length of infection or the anatomical site of the nodules; however, it is correlated *with the number of nodules present* (*i. e.*, *it is significantly a more common association when 5 or more nodules exist* (Puig Solanes *et al.*, 1948)

Acute ocular symptoms, which are associated with an erysipelatoid

condition of the ears, nose, etc., include particularly intense photophobia, blepharospasm and lacrymation, all resulting from vascular injection caused by the discharge of the parasite's toxins. More advanced changes include vascular congestion and pigmentation of the conjunctiva, punctate keratitis of the cornea, iritis, chorioretinitis, retrobulbar neuritis and optic nerve atrophy (Scott, 1945).

The microfilariæ, which migrate out through the fibrous capsule of the nodules, especially those on or near the temples or scalp, travel through the surrounding tissues, probably most frequently through lymphatic vessels and rarely, if ever, through the blood vessels to various organs and tissues of the body, including the eye. They have been observed in considerable numbers in the conjunctivæ, cornea and sclera and are very abundant in the tissues surrounding the optic nerve, but they are sparce or even rare in the iris and retina. Their presence and location are not sufficient to account for the degree of ocular damage produced in the infection, particularly in the iris and deeper membranes which are primarily responsible for loss of visual acuity (Puig Solanes *et al.*, 1948). The lesions produced consist of petechial hemorrhage, inflammatory perivascular infiltration, edema and pigmentation of the various tissue layers, punctate, vascular and interstitial keratitis, and, terminally, fibrosis of the cornea and atrophy of the optic nerve. The majority of these proliferative and degenerative changes can be observed ophthalmoscopically.

In Guatemala, and occasionally in other endemic areas, patients with no visible or palpable *Onchocerca* tumors may have symptoms of disturbed vision (Adams, 1938). Other patients from whom all visible nodules have been excised develop faulty vision years afterwards. Some of these patients also exhibit hypersensitivity to tactile stimuli (personal demonstration by Dr. R. Robles to the author, 1938). In these patients the microfilariæ can usually be demonstrated in biopsied pieces of skin or corneal conjunctiva. These observations, based primarily on white patients who have contracted the infection in endemic foci, support the view that some parent worms in the subcutaneous tissues either failed to stimulate fibrous encapsulation, or are located in nodules not superficially visible or palpable.

A certain proportion of cases shows painful erysipelatoid swellings of the face and scalp, and particularly of the ear-lobes. The tumefactions of the head are frequently accompanied by a marked elevation of temperature. In Guatemala this variety of the disease is referred to as "Coastal erysipelas."

Diagnosis.—From a diagnostic view point the following types of onchocercosis are recognized: (1) Visible or palpable nodule but biopsy of skin negative for microfilariæ due to (a) immaturity of the parent worms, (b) females mature and discharging microfilariæ but these embryos still within the nodule, or (c) females ... and mature but without males, hence not producing embryos; (2) ... edema and inflammation of ... toid variety), with microfil... but not flushed or ... nodules present, skin thick and purplish but not flushed or tender, ... nodules present, skin thick and purplish but not flushed or ... nodules of different maturities present, microfilariæ demonstrable, and (4) ... patient with an onchocerchosis facies indicating premature aging, micro-

filariæ demonstrable, and (5) any of the above types with different degrees of involvement of the eye. In endemic foci the presence of nodules of the types described above *is suggestive of onchocercosis, but these nodules must* be distinguished from lipomas and other types of nodules. Excision of the nodules under local novocaine anesthesia, their gross section and demonstration of the delicate thread-like worms in the matrix of the tumor

small pieces of skin or,

, *provides material from*

p of tepid physiological

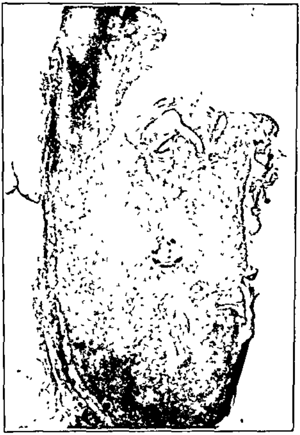


FIG. 274.—Section through nodule in *Onchocerca volvulus* infection, showing sclerosed outer layer, fibro-mucous matrix, and worms imbedded in matrix. × 6. (Original photomicrograph of section prepared from material presented to the author by Prof. F. Fülleborn.)

salt solution and demonstrated under the microscope. Puncture of the cysts to obtain *microfilariæ for diagnosis is not advised since this may kill* the parent worms and produce a severe allergic condition. In patients without palpable nodules, but otherwise having symptoms suggestive of onchocercosis, demonstration of the microfilariæ from the skin or conjunctiva constitutes the only certain method of specific diagnosis. Unlike the other well-known microfilariæ in man, those of *Onchocerca* invade the blood vessels so rarely, if ever, that blood examination is not a practical

method of diagnosis. A moderate to high eosinophilia (12 to 75 per cent) may suggest a helminthiasis and thus indirectly lead towards a specific diagnosis. Although Van Hoof (1934) demonstrated a positive complement-fixation test in this infection, workers had little success in Africa in utilizing this diagnostic aid, but Bozicevich *et al.* (1947) have employed *Onchocerca*, *Dirofilaria immitis* and other filarial antigens with relatively satisfactory results in intradermal and complement-fixation tests of American patients.

Therapeusis.—Many chemotherapeutics have been tried in attempts to kill the Onchocercas but until recently (1947) none have been particularly promising. Antihelmintics like neostibosan and neoantimosan introduced [illegible] ... produced for some time. Clinical tests with Naphuride sodium (Bayer 205) in two small series in Guatemala and Mexico have provided some evidence that the drug, in an amount of 0.02 Gm. per kilo every week for 8 weeks, not only inhibits production of microfilariæ but kills some or all of the worms. Similarly, in both of these areas, limited clinical trial has been made of Hetrazan (1-diethyl-carbamyl-4-methylpiperazine HCl), but the doses of 1 to 2 mgm. per kilo of body weight tolerated by *W. bancrofti* patients have proved so toxic for *Onchocerca* patients that the amount has of necessity been reduced to a fraction of the trial doses. A possible explanation is that Hetrazan kills the worms rapidly and produces a profound allergic state. Introduction of filaricidal drugs directly into the center of the nodule housing the parent worms may occasionally kill them, but this procedure is painful and is not always reliable, although it is recommended by Rodhain and Valcke (1935) and d'Hooge (1935).

The simplest and most satisfactory treatment thus far devised is to enucleate the nodules as soon as they appear.

Prognosis.—Usually good in those patients in whom the microfilariæ do not endanger the vision, but in a considerable proportion of cases in Guatemala and Mexico eye pathology is already present when the patient is first examined.

Control.—The breeding habits of the intermediate host, *Simulium*, under stones in fast-flowing streams, makes larvicidal control of this host difficult. Certain workers have advocated the installation of barrels of oil containing larvicidal chemicals at sites above the breeding grounds, so that the oil will be slowly discharged into the stream. A more practical plan is the incorporation of concentrates of DDT into blocks of cement, which are then placed in the stream above the breeding grounds. This latter method has been tested in the Belgian Congo with considerable success (*fide* Dr. Louis van den Berghe).

In highly endemic areas considerable control may be effected by removing all of the palpable nodules as soon as they appear, thus reducing the likelihood of systemic intoxication produced by the worms in the tissues, the danger of ophthalmic damage and, at the same time, preventing the gnats from becoming infected. As a precautionary measure infected patients should not be allowed to travel into uninfected territory where the susceptible *Simulium* hosts occur.

Genus Acanthocheilonema Cobbold, 1870

(genus from ἄκανθα, spine, χεῖλος, lip, and νῆμα, thread)

Acanthocheilonema perstans (Manson, 1891), Railliet, Henry and Langeron, 1912. (The persistent filaria.)

Synonyms.—*Filaria sanguinis hominis minor* Manson, 1891; *Filaria sanguinis hominis perstans* Manson, 1891, *Filaria ozzardi* var *truncata* Manson, 1897, *Dipetalonema perstans* (Manson, 1891) Yorke and Maplestone, 1926.

Historical and Geographical Data.—This species of filarioid nematode was discovered by Daniels in Demeraran aborigines in British Guiana and was first described and named by Manson, who also first identified the microfilariæ in the blood of Negroes from the Congo. Since that day the infection has been found to be preva-

filaria relatively common in Northern Rhodesia where *W. bancrofti* is uncommon and *Loa loa* is not known to occur. It has also been reported from western coastal

Amazon Valley and in
ıea, Algiers and Tunis
itish Guiana where the
requently associated in
id of *Loa loa*, in South

America, at times with that of *Mansonella ozzardi*. Stoll (1947) has estimated the world incidence of *A. perstans* as 27 millions, including 19 millions in Africa and 8 millions in tropical America

Man is the only important definitive host of *A perstans*, although *Pan satyrus* and other higher primates in Africa have been listed as hosts. Several related species of this genus and closely related genera have been recovered from monkeys from the Western Hemisphere (Faust, 1935; McCoy, 1935, 1936)

Structure and Life Cycle of the Worm.—The adult worms are long, cylindrical, filiform nematodes, with a smooth cuticula and a simple, unarmed, oral extremity, covered with a cuticular shield bearing on each side a large lateral and a pair of submedian papillæ (Fig 275 *A*). The tail in both sexes is recurved ventrad, and the cuticula of the extreme caudal tip is split, so as to form a pair of minute triangular flaps, which are devoid of a supporting core (Fig. 275 *B*)

The male measures 45 mm. in length by 60 μ in greatest breadth, with a cephalic diameter of 10 μ In the cloacal region there are 4 pairs of preanal papillæ and 1 postanal pair The copulatory spicules are rod-like and very unequal in length (Fig. 275 *C*)

The female has a length measurement of 70 to 80 mm and a greatest breadth of 120 μ, while the diameter of the bluntly rounded head is 70 μ. The vulva is situated 0.6 mm from the cephalic end.

The adult worms live in the body cavities and associated tissues, including the mesentery, the perirenal and retroperitoneal tissues, the pleural cavity and the pericardium, where they are sometimes found in considerable numbers.

The microfilariæ of *A perstans* are non-periodic, but their numbers in the blood vary at different times. They have a greater predilection for concentration in the heart, lungs and greater arteries than for the peripheral

circulation. These microfilariæ (Fig. 275 *D*) measure about 200 μ by 4.5 μ, and are capable of remarkable contraction and elongation. They are conspicuously smaller than the microfilariæ of *Wuchereria bancrofti* [illegible] *Loa loa*, and lack a "sheath" (*i. e.*, [illegible] tion or shortly thereafter). The h[illegible] body which ends in the tail begins some distance anterior to the equatorial plane. There is no cephalic lancet. The excretory pore is about 30 μ from the head end and the anal pore is inconspicuous. The genital cells are difficult to demonstrate. In addition to the ordinary wiggling movement characteristic of all microfilariæ, this organism also travels about through the blood as the microfilariæ of *Wuchereria bancrofti* do in the mosquito's stomach. A period of development in an intermediate insect host is necessary before the worms become infective again for man. Only partial

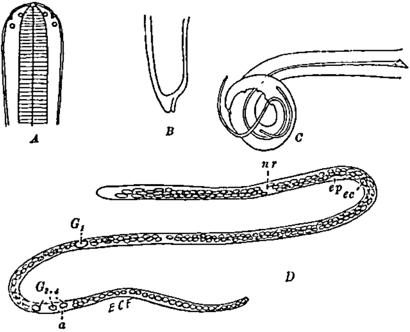


FIG 275 —*Acanthocheilonema perstans*. *A*, anterior end of worm, with papillæ; *B*, caudal end of female worm, with cuticular flaps, *C*, caudal extremity of male worm, showing caudal papillæ and copulatory spicules, *D*, microfilaria from peripheral blood of patient. *a*, anal pore; *ec*, excretory cell, *ep*, excretory pore, G_1, G_{2-4}, so-called "genital cells", *nr*, nerve ring. (*A*, *B*, *C*, after Leiper, Trans Roy Soc. Med. and Hyg , *D*, × 888 original)

development has been obtained in *Culex pipiens* subsp., in *Mansonia uniformis* and in *Anopheles maculipennis* subsp., while Sharp (1928) has obtained complete development in *Culicoides austeni*, including: migration through the wall of the stomach and hemocele to the thoracic musculature; metamorphosis within twenty to thirty hours into a true first-stage larva; two (and possibly more?) ecdyses during residence in the thoracic muscles; then migration through the softer structures of the head into the labium, and emergence of mature larvæ from the proboscis seven to ten days after experimental infection of the flies. About 7 per cent of the wild *C. austeni* at Mamfe, Cameroons, were found naturally infected. The related species, *C. grahami*, is probably an equally good intermediate host.

The incubation period in man is not known.

Epidemiology.—Human infection results from inoculation with the infective larvæ at the time the *Culicoides* takes a blood meal. In turn, the fly becomes infected from ingesting *Microfilaria perstans* at the time it takes a blood meal from man. The infection occurs in tropical regions of Africa and the Americas.

Pathogenesis, Pathology and Symptomatology.—The parent worms live in body cavities. In certain individuals the presence of the worms and their metabolites may occasion a moderate allergic state, with eosinophilia, edema and possibly asthma. Bourguignon (1937) found numbers of *Mf. perstans* in liver tissue, in association with necrotic foci presumably of bacterial origin. Certain workers in endemic areas would assign to the worm the causative rôle in certain cases of lymph varix. Morenas (1929) reported the presence of this filaria in a patient who had toxic edema of the left eyelid, dyspnea, precordial pain and had a 50 per cent eosinophilia. In *A. gracile* infection in New World monkeys the worms characteristically sew themselves into the mesentery, epiploon, pleura and pericardium and provoke a pronounced fibrinous exudative reaction.

Diagnosis.—On finding non-periodic microfilariæ of this specific type in peripheral blood.

Therapeusis.—No specific treatment is known.

Prognosis.—Good.

Control.—This filaria, although widely distributed, appears to be dependent on intermediate insect hosts which breed only in forest, jungle or swamp. The gradual reduction of such areas will probably be accompanied by a corresponding diminution in infection with *Acanthocheilonema perstans.*

Acanthocheilonema streptocerca (Macfie and Corson, 1922) comb. nov.

Synonyms.—*Agamofilaria streptocerca* Macfie and Corson, 1922; *Microfilaria streptocerca* (Macfie and Corson, 1922) Stiles and Hassall, 1926; *Dipetalonema streptocerca* (Macfie and Corson, 1922) Peel and Chardome, 1946.

The microfilaria of this worm was first described by Macfie and Corson from biopsy of natives of the Gold Coast, where *Onchocerca volvulus*, *A. perstans* and other human filarias occur. It was present in 44 per cent of a surveyed group, all of whom were in apparent good health. In 1938 one native of the Belgian Congo was found to harbor this species of filaria and in 1939 three additional human infections were discovered. In 1946 Peel and Chardome for the first time discovered adults (two females and a fragment of another), in the cutaneous connective tissue of *Pan paniscus* and *Pan satyrus*.

The microfilariæ are sheathless and taper at both extremities. When fixed, the body is relatively straight except at the posterior end which is strongly bent in a shepherd's-crook curve. They range in length from 180 to 240 μ and measure about 3 μ in diameter. The anterior extremity is bluntly rounded. No oral stylet has been seen. The anatomical landmarks which have been found are as follows (expressed in percentage distance from the anterior end): nerve ring, 26.9; excretory pore, 34.1; G_1-cell, 69.2; anal pore, 86.2. The posterior extremity is blunt and contains

ovoidal nuclei to within 1 μ of the end. Sharp (1927) has found that the capacity of this microfilaria for vital dyes is very slight, like that of *Wuchereria bancrofti*, as contrasted with the strong affinity of the microfilariæ of *O. volvulus*, *Loa loa* and *A. perstans*. According to Sharp, this species does not utilize *Simulium damnosum* as an intermediate host.

Workers in the Belgian Congo state that in some infected individuals there is considerable cutaneous edema and elephantiasis of the skin for which the worms are possibly responsible.

Rao (1931) described a new microfilaria (*Mf. actoni*) from eastern India. This embryo, said to be related to *Mf. perstans*, is sheathless, exceedingly small and has terminal tail nuclei.

Genus Mansonella Faust, 1929

(genus named for Sir Patrick Manson)

Mansonella ozzardi (Manson, 1897) Faust, 1929. (Ozzard's filaria.)

Synonyms.—*Filaria ozzardi* Manson, 1897 (*pro parte*); *Filaria Demarquayi* Manson, 1897 (*nec* Zune, 1892); *Filaria juncea* Railliet, 1918; *Filaria tucumana* Biglieri and Aráoz, 1917.

Historical and Geographical Data.—This filaria was first studied in the microfilarial stage by Manson, in blood obtained by Ozzard from Carib Indians from the interior of British Guiana. The microfilaria was at first believed to be different from that obtained by Newsam from natives of St Vincent, which was designated *F. demarquayi* by Manson, but the studies of Penel and of Leiper have shown that the two forms are identical. Since the name *demarquayi* was previously used by Zune (1892) for another human microfilaria (possibly *Mf. bancrofti*), it is not available for Manson's species, which becomes *M. ozzardi* The distribution of this species includes the northern states of Argentina, inland along the northern coast of South America (McCoy, 1933; Buckley, 1934; Rounti, 1935), Yucatan (C. C. Hoffmann, 1930) and certain of the British West Indies (St. Vincent, St. Lucia, Dominica) In Colombia and southeastern Panamá the coastal areas more frequently show *Acanthocheilonema perstans*, while the river valleys farther inland more characteristically have a heavy *Mansonella ozzardi* infection (McCoy, 1933). The microfilaria, which is found in 25 to 30 per cent of the natives of the northern states of Argentina and has been described as *F. tucumana*, is the same species (Vogel, 1927) Manson, as well as Seligmann, report this species from New Guinea, but this latter may be "*Filaria*" *malayi* or some other species.

Structure and Life Cycle.—In *Mansonella ozzardi* the male is known only from a single posterior fragment of 38 mm., with a maximum diameter of 0.2 mm. The tail is strongly recurved, and becomes gradually narrowed up to 0.27 mm. from the extremity, where it abruptly rounds off into a slightly bulbous termination. The two copulatory spicules, presumably unequal, have not been described in detail.

The female has a length of 65 to 81 mm. and a maximum breadth of 0.21 to 0.25 mm. The cuticula is smooth. The head is unarmed. The small mouth leads directly into the esophagus. The anal opening is on the summit of a small papilla, 0.25 mm. from the posterior extremity. On either side of the caudal extremity [illegible] lappets with a fleshy core (Fig. 276 *A*). The vul[illegible] anterior end of the female worm. [illegible]

more or less irregular in contour as it proceeds to the junction with the two uterine tubes. The small ovoidal eggs measure 21 by 8.4 μ. Various stages of development are found in successive parts of the uteri from within outwards. The fully-developed microfilaria escapes from the egg membrane before oviposition takes place, so that the microfilaria is "unsheathed."

This microfilaria (Fig. 276 *B*) is very active in fresh blood-films, elongating and constantly coiling on itself. It measures about 185 to 200 by 5 μ. The cephalic extremity is provided with a poorly-developed prepuce. The caudal end is pointed to somewhat the same degree as that of *Microfilaria perstans* Both the oral and the caudal extremities are free of nuclei (2 2 to 2 5 per cent and 98 0 to 98.2 per cent respectively). The nerve ring is situated between 21.9 and 22.2 per cent distance from the anterior extremity. The excretory pore is situated at about the junction of the anterior and the equatorial thirds of the body (30.9 to 31 5 per cent) with the excretory cell just posterior in position (35.0 per cent) The G_1 cell is at 67.9 to 69 3 per cent and the G_4 cell at 79.2 per cent, the latter being immediately in front of the anal pore (79.4 per cent). The microfilariæ of this species are non-periodic. According to Low and Vincent, *Aëdes ægypti* (*syn. Stegomyia fasciata*) was believed to be the insect host, while Fulleborn obtained

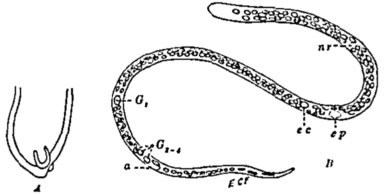


FIG. 276 *Mansonella ozzardi* *A*, posterior extremity of female, enlarged (after Leiper, Trans Royal Soc of Med and Hyg) *B*, microfilaria, × 888 *a*, anal pore, *ec*, excretory cell, *ep*, excretory pore, G_1, G_{2-4}, so-called "genital-cells", *nr*, nerve ring (Original)

and 5 per cent of the wild flies of this species were naturally infected Within twenty-four hours after ingestion by the fly in a blood meal the embryos have migrated to the thorax, in the musculature of which metamorphosis, through three true larval stages, with two ecdyses, occurs. Complete development to the infective-stage larvæ and migration of these larvæ through the tissues of the head to the tip of the proboscis take place within five to seven days

Epidemiology.- In endemic territory man acquires infection following exposure to mature larvæ of the worm which are deposited on the skin

when an infected appropriate species of *Culicoides* takes a blood meal. The gnat acquires infection from persons in whose blood the microfilariæ are circulating.

Pathogenesis, Pathology and Symptomatology.—The adult worms have been recovered from the mesentery and the subperitoneal tissue of the anterior abdominal wall. The worms are believed to be non-pathogenic. No symptoms have been recorded, but in certain individuals there is the possibility that the worms may be responsible for allergic manifestations.

Diagnosis.—On the discovery of microfilariæ of this species in peripheral blood. They must be differentiated from *Mf. bancrofti* and *Mf. perstans*, with which they are frequently associated, and from *Mf. malayi*, which is "sheathed" and has nuclei in the caudal tip.

Therapeusis.—Unstudied.

Prognosis.—Good.

Control.—Unstudied. Undoubtedly involves protection of individuals in endemic areas from "bites" of *Culicoides* and the more general problem of gnat eradication.

Subfamily Dirofilarinæ Wehr, 1935

(Synonym: Loainæ Yorke and Maplestone, 1926, *pro parte*)

This subfamily contains species in which the caudal alæ are well-developed, supported by pre-anal and post-anal pedunculated papillæ. Species of this group which have been reported from man include: *Dirofilaria magalhãesi* (Blanchard, 1896), *D. repens* Railliet and Henry, 1911, *D. louisianensis* Faust, Thomas and Jones, 1941, *D. conjunctivæ* (Addario, 1885) and *Loa loa* (Cobbold, 1864).

Genus Dirofilaria Railliet and Henry, 1911

(genus from *dirus*, cruel, and *filaria*)

The members of the genus *Dirofilaria* are characterized by the lack of oral labia and by possessing very inconspicuous cephalic papillæ. The esophagus is relatively short and is divided into an anterior muscular and a posterior glandular portion. The spirally-coiled posterior extremity of the male worm has a bluntly conical termination and is provided with caudal alæ. There are large pedunculated pre-anal, and small post-anal papillæ, the spicules are unequal, and a gubernaculum is wanting. The vulva of the female worm is slightly post-esophageal in position. The embryos hatch before they escape from the mother worms and the "unsheathed" microfilariæ circulate in the blood. The adult worms of these species live in the chambers of the heart and connective tissue of various mammals. The most common species is *Dirofilaria immitis* (Leidy, 1856), [illegible]

[illegible]

Subgenus Dirofilaria Faust, 1937

[illegible]

copulatory spicules is not distinctly acuminate. They live in the chambers of the heart.

Dirofilaria Magalhãesi (Blanchard, 1896 *nec* 1895), Railliet and Henry, 1911.

Synonyms.—*Filaria magalhãesi* Blanchard, 1896; *Filaria bancrofti* de Magalhães, 1892.

The only reported case of this infection was that of de Magalhães, who, in 1887, recovered one male and one female specimen from the left (?) ventricle of a Brazilian child The male measured 83 mm long by 0.407 mm. in diameter The tail was coiled 540 degrees. There were 4 pairs of pedunculated prominences, and 4 pairs of postanal papillæ, all of which were described as "mulberry-shaped," with superficial denticulations. Of the two unequal spicules the lesser had a length of 230 μ The cloacal [illegible]
measure [illegible]
2.56 mm. from the anterior end [illegible]
from the rounded posterior extremity The cuticula of the worms was opaque, white, and transversely striated

The embryos coiled in the egg membrane *in utero* measured 38 by 14 μ At the time of oviposition, they escaped from the "sheath" The length measurement of these microfilariæ was 0 3 to 0 35 mm and the diameter 6 μ. Their cuticula was provided with delicate, transverse striations

Although the life cycle of the organism has not been studied it is conceivable that a mosquito serves as an intermediate host, in a way similar to that described by Fulleborn for *Dirofilaria immitis*

A male *Dirofilaria* (subgenus) *Dirofilaria*, with characters specifically different [illegible] nchard, 1896), was [illegible] Negress, native and [illegible] 941) designated this worm as *D louisianensis* for purposes of record, although a revision of the subgenus *Dirofilaria* may justify the inclusion of *D magalhãesi* and *D louisianensis* in the species *D immitis*

Subgenus Nochtiella Faust, 1937

Members of this subgenus are relatively small filariæ The males have a distinct asymmetry in number and distribution of their caudal papillæ and a very acuminate larger spicule. Species of this subgenus live primarily in the cutaneous and subcutaneous tissues

Dirofilaria repens Railliet and Henry, 1911

Synonym.—*Filaria acutiuscula* Molin, 1858, of Chitwood, 1933.

This worm has been recovered as a natural parasite of dogs in Europe (Italy), the U S S R, Indo-China, Argentina, Brazil and the United States (Desportes, 1939–1940) A single human infection has been reported (Skrjabin *et al*, 1930) A male worm was removed from a subcutaneous nodule of the lower right eyelid of a female patient in the U S S R

Male worms removed from the canine host measure 5 to 7 cm in length by 0 37 to 0 45 mm in diameter There are 2 to 4 adanal papillæ on one side and 5 or 6 on the other The longer, acuminate spicule has a length of 0 465 to 0 590 mm , the shorter one, 0 185 to 0 206 mm.

Female worms m [illegible]
vulva is situated 1 [illegible]
207 to 360 μ by 5 to [illegible]
Aedes ægypti, *A communis* and *Anopheles maculipennis maculipennis* have been found to be acceptable intermediate hosts

The percentage distance of the microfilaria's landmarks from the cephalic extremity are as follows nerve ring, 20 1; excretory pore, 29 2, G_1 cell, 63 0, anal pore, 75 7, terminal caudal nucleus, 89 6.

Dirofilaria conjunctivæ (Addario, 1885) Desportes, 1939-1940.

Synonyms.—*Filaria conjunctivæ* Addario, 1885; *F. labialis* of Pierantoni, 1907 (nec *F. labialis* Pane, 1864, = *Gongylonema*, *fide* Sambon, 1924 and Brumpt, 1927); possibly *F. palpebralis* Pace, 1867; *F. peritonæi-hominis* Babes, 1879; *F. inermis* Grassi, 1887; *F. apapillocephala* Condorelli-Francaviglia, 1892; *I*

Immature filariæ w

the one described by

filaria, have been reported on numerous occasions from the Mediterranean Basin, as well as other localities. These include the following: An adolescent filaria, 14 cm. long (*F. peritonæi-hominis* Babes, 1879), removed from a nodule in the gastrosplenic ligament, at autopsy of a woman in Budapest, an immature female worm, 10 cm. long (*F. palpebralis* Pace, 1866), removed from the upper lip of a boy

tumor in Palermo (Supino,

(Alessandrini, 1906); two se

an immature male worm was recovered (Forbes, 1918); one from the eye of a man in Argentina (*Filaria* sp., Parodi and Bonavia, 1920); one incomplete female worm obtained from a conjunctival tumor, superior orbital location, from a resident of Narbonne, France (Coutelan, Joyeux and Artigues, 1933); two additional cases from France, one from Central Africa (de Meillon and Gillespie, 1943), and one from Turkey (Unat, 1944).

Desportes (*l. c.*) states that all of the worms recovered from the Mediterranean Basin are species of *Dirofilaria*, because they have a relatively short esophagus, a short tail and a patent anus; that on account of their anatomical position in man they closely conform to *D. repens* (*i. e.*, belong to the subgenus *Nochtiella* Faust, 1937), but that they appear to be specifically distinct.

D. conjunctivæ is an encysted subcutaneous-tissue parasite, of which several females and one male have been recovered. The female measures 16 to 20 cm. in length by 0.5 mm. in breadth The male has a length measurement of 58 mm. The cuticula is finely striated. The oral end is unarmed, the anus subterminal (0.3 mm. from the caudal extremity) and the vulvar opening of the female 50 to 104 μ from the anterior extremity. The uterus is composec filled with embryos measuring 250 μ by 55μ. The infec

and, at times, a localized

The life cycle of *D. conjunctivæ* is known only in so far as the worms in man are concerned. First of all it is necessary to obtain mature males in order to ascertain if the species is distinct from other species of the genus. Secondly, since man does not appear to be an entirely suitable host (*i. e.*, the worms do not reach maturity in human tissues), it is important to discover the reservoir of the infection. In the third place, the microfilariæ must be discovered and their characters carefully studied. Finally, the arthropod transmitter must be found and the developmental stages of the parasite described. It seems probable that mosquitoes are the natural intermediate hosts of *D conjunctivæ* as they are for *D. immitis* and *D. repens*, but this requires demonstration.

Genus Loa Stiles, 1905

(genus from *loa*, a term commonly used by the natives of Angola, West Africa, for the worm)

(The loa worm or "eye worm," producing loaiasis or fugitive swellings.)

Loa loa (Cobbold, 1864) Castellani and Chalmers, 1913. (The loa worm, producing loaiasis.)

Synonyms.—*Filaria medinensis* Gmelin, 1788 *pro parte*, *Filaria oculi humani* Dujardin, 1845; *Filaria lacrymalis* Dubini, 1850 *nec* Gurlt, 1833, *Filaria oculi* Gervais and van Beneden, 1859, *Dracunculus oculi* Diesing, 1860, *Filaria subconjunctivalis* Guyon, 1864 of Braun, 1902, *Dracunculus loa* Cobbold, 1864, *Filaria loa* Guyot, of Leuckart *et al.*, Embryo *Microfilaria diurna* Manson, 1891.

Historical and Geographical Data.—The earliest record of the loa worm was that of Mongin (1770) who extracted a specimen from between the conjunctiva and albuginea of a Negress at St Domingo (Haiti). There followed a series of cases described from the New World by Bajon (1777, Cayenne, F. Guiana), Arrachart (1805, St Domingo), Larry (1812, St Domingo), Roulin (1828, Magdalena R., Colombia), Guyon (1838, Martinique), Lallemant (1844, Rio de Janeiro), and others All of these cases were recently imported West African slaves The first authentic observations of the presence of the species in indigenous territory were those of Guyot (*ca* 1777) in Angola, where the worm was stated to be a common human infection, and was described under the native name of *loa* Since these earlier observations the distribution of *Loa loa* has been found to be quite extensive in Central West Africa, being distributed along the coast from Southern Nigeria, the Cameroons, down to Angola, and from the French Congo inland to Central Tropical Africa (Welle River district) and possibly to the contiguous border of

an incidence of 90 per

e New World are now

African endemic areas

Stoll (1947) has estimated the world incidence of loaiasis to be 13 millions, all acquired in Africa

Structure and Life Cycle.—The adult worms were first carefully studied by Looss (1904). The body is cylindrically filiform and semitransparent, tapering anteriorly to the small terminal mouth, which lacks papillæ. The head, is, however, ornamented with two lateral and four small submedian papillæ (Fig 277 A), which lie in one transverse plane just behind the mouth.

The males measure 30 to 34 mm in length by 0.35 to 0.43 mm in greatest breadth, which is in the anterior part of the body. The posterior portion tapers gradually towards the caudal end The females range from 50 to 70 mm. in length, and have a maximum diameter of about 0.5 mm. The cuticula is provided with numerous rounded, smooth, translucent bosses, varying greatly in number and arrangement. In the male they are lacking at the two extremities, but in the female they are commonly present at the posterior end and may also be found at the cephalic extremity The mouth opens directly into a slender muscular esophagus Posterior to the esophagus is the long filiform mid-intestine, which attains a diameter of 65 μ and is continued at its caudal extremity into a short attenuate rectum

The tail of the male (Fig 277 B, C) is curved somewhat ventrad It is

provided with lateral alate expansions of the cuticula. The cloacal opening lies mid-ventral in position, about 80 μ from the posterior end of the worm. It is surrounded by 5 pairs of asymmetrically placed pedunculated papillæ, while about 3 pairs of small sessile papillæ are situated towards the caudal tip. The two copulatory spicules are unequal, measuring 123 to 176 μ and 88 to 113μ respectively. The ano-genital orifice is guarded by a powerful sphincter.

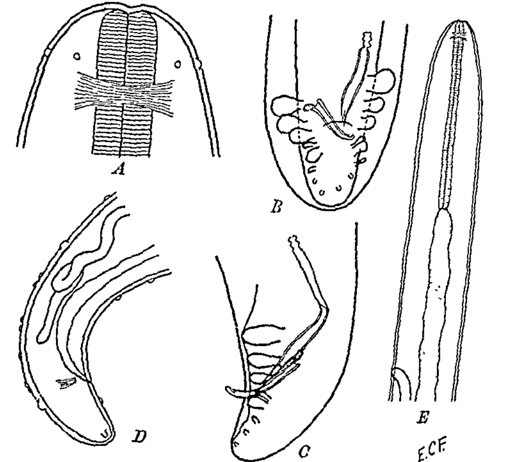


FIG. 277.—*Loa loa.* *A*, anterior extremity of body, showing lateral and submedian papillæ; *B*, posterior end of male worm, ventral view, showing caudal alæ, papillæ and copulatory spicules, *C*, lateral view of male worm *D*, caudal extremity of female worm, lateral view, … ; *E*, anterior end … *A*, *B*, *C*, × 180, … Maplestone, Nematode Parasites of Vertebrates, courtesy of J. and A. Churchill.)

The posterior end of the female (Fig. 277 *D*) is broadly rounded and has a pair of terminal papillæ. The vulvar opening in the female is situated some 2.5 mm. from the anterior end (Fig. 277 *E*). The vagina extends posteriad for a distance of 9 mm., where it bifurcates to form the uteri. These latter, with their inner receptacula seminis, oviducts, and ovarian-tubule continuations, practically fill the entire body. The uteri contain all stages of the developing embryos, which are enclosed in an egg membrane. This membrane in the fully embryonated egg becomes elongated into the "sheath" which surrounds the microfilaria.

According to Coutelen (1935) the length of life of the adult *Loa loa* varies from four to fifteen years.

The microfilariæ, which are discharged into the subcutaneous and deeper cutaneous passages formed by the worms in their migrations, reach the peripheral bloodvessels, in which they are most commonly found during certain parts of the day (9 A.M. to 2 P.M.). This phenomenon has been responsible for the designation of these embryos as *Microfilaria diurna.* The microfilariæ are similar in size (250 to 300 μ by 6 to 8.5 μ) to the corresponding embryos of *Wuchereria bancrofti* but differ specifically in internal organization. These points of difference were first carefully studied by Fülleborn (1913). They are illustrated in the accompanying figure (Fig. 278). Sharp (1923) made a careful comparison in both living and fixed microfilariæ and found that they were stiff and ungraceful but could move rapidly across a microscopic slide by a combination of lashing and undulating movements. The caudal end is short and relatively thick and the cephalic end broad and flat. (For comparison with *Mf. bancrofti* and *Mf. malayi*, *vide* Table 3, p. 504.)

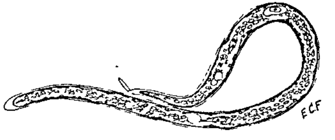


FIG. 278.—Microfilaria of *Loa loa* For explanation of landmarks see Fig 260 × 666. (After Fülleborn, Archiv f Schiffs- u Tropen-Hygiene)

The life cycle of *Loa loa* involves certain species of mango flies (*Chrysops dimidiata*, *C. silacea* and possibly other species of this genus), which are day-feeders. As early as 1895, Manson suggested on epidemiological grounds that *Chrysops dimidiata* was the intermediate host of the worm. The work of Leiper on the West Coast of Africa in 1912–1913 lent certain experimental proof to this view, while at the same time it showed that other "biting" insects were probably unsuitable hosts. Leiper's experiments were confirmed by Kleine (1915), who investigated the problem in the Cameroons. Finally the detailed transmission studies of the Connals (1921–1922) have given a complete history of the insect phase of the life cycle.

The microfilariæ are taken into the stomach of *Chrysops* when the fly takes a blood-meal of a patient harboring the microfilariæ in his peripheral blood. Shortly after being ingested, the embryos break their way out of their "sheaths." They then increase somewhat in size, make their way through the stomach wall, and proceed to the muscular and connective tissue of the abdomen and to a lesser degree the tissues of the thorax, where they become thickened and bent on themselves, while the caudal extremity develops a sickle-shaped termination. During the third day the alimentary tract becomes complete. From the fourth day increase in length takes place and by the fifth day the larva is usually coiled into a corkscrew spiral.

[illegible] curves. The [illegible]

[illegible] which occurs in the intermediate host. From the seventh day onwards a marked increase in length occurs, accompanied by a slight decrease in breadth. The larvæ now migrate to the fly's head, where the mature ones may be found in largest numbers about the tenth day. These larvæ measure 2 mm. in length by 25 to 27 μ in breadth. The worms are now ready to leave the fly when the host takes a blood-meal. They make their way rapidly down through the labium, and emerge as white glistening threads, their numbers in heavily infected flies amounting to several hundred. While most of the mature larvæ leave the dipteran host in one migration on or about the tenth day, the fly may remain infective for a period of five days. Within sixty seconds after the worms have emerged from the fly they have disappeared under the skin of the mammalian host. Attempts to infect monkeys, rabbits and guinea-pigs have been unsuccessful, although the larvæ readily penetrate the skin of the guinea-pig.

Nothing is known of the development of the worms once they have reached the subcutaneous areas of the human host.

Epidemiology.—Man becomes infected from the "bites" of certain species of *Chrysops* harboring the infective-stage larvæ of this filaria. White persons in endemic areas are usually less frequently exposed to "bites" of *Chrysops* and, therefore, even if they become infected, harbor relatively fewer worms than the native population. The fly becomes infected from blood meals of patients having *Mf. loa* in their circulating blood. The flies are phototactic and characteristically feed during the daytime.

Pathogenesis, Pathology and Symptomatology.—The adult worms ordinarily live in the subcutaneous connective tissue of man, where they migrate back and forth, for the most part without causing serious symptoms. They have been found in the extremities, the trunk and even the scrotum, but appear to have a certain predilection for the head. They have been recovered from the frenulum linguæ, the vicinity of the epiglottis and especially from the region of the conjunctivæ. They have even wandered into the anterior chamber of the eye. They are temporarily bothersome when passing across the front of the eyeball (Fig. 279), just beneath the corneal conjunctiva, or over the bridge of the nose. Likewise, most cases give a history of fugitive swellings (Calabar swellings), which may become as large as a half goose-egg, are painless but hot, do not pit, and disappear in two or three days. The exact relationship of the worms to these ephemeral swellings remains unexplained, but it is believed to be a phenomenon of temporary local sensitization.

Van den Berghe (personal communication) recognizes three clinical types of loaiasis, viz., (1) patients in whom adults and microfilariæ are found without m[illegible] patients positive for the adults and [illegible] pruritus and eosinophilia, and (3) pa[illegible] recovered and migrating adults are not evident but with marked edema and pruritus, recurrent fever and eosinophilia. Dubois (1946) described this third type for

Europeans and indicated that the syndrome frequently consisted of pruritus, filarial edema, prurigo, thickening of the skin and eosinophilia. Johnstone (1947) reported on a personal infection with four mature worms. The symptoms consisted of pitting edema and associated severe neuralgia of the affected member; on return to England the fugitive swellings were much more pronounced during the warm summer months than in winter. During its spontaneous emergence from the inner canthus of the eye one worm caused acute pain.

Diagnosis.—In a patent infection this is made on recovery of one of the

intradermal test (Chandler, Milliken and Schuhardt, 1930; Rodhain and Dubois, 1932), although this usually indicates only that the patient has a filarial infection. In persons with allergic manifestations but without adults or microfilariæ, the intradermal test provides evidence of filariasis. On the basis of exposure and clinical grounds differentiation must then be made from other types of filariasis.

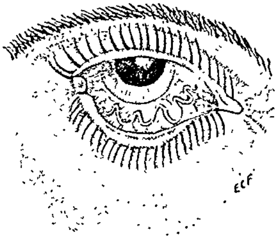


Fig. 279 Diagram illustrating the migration of the adult *Loa loa* through the corneal conjunctiva. (Original)

Therapeusis.—There is no eminently satisfactory chemotherapy for loaiasis. *De Choisy (1937) obtained relief from the fugitive swelling in one* patient after eleven injections of a 6 per cent solution of lithium antimonyl thiomalate in amounts of 2 to 4 cc. approximately every other day. Pentavalent antimonials, as neostibosan, also Naphuride sodium and Hetrazan all deserve special clinical trial. (*Vide supra* under "*Wuchereria bancrofti*" and "*Onchocerca volvulus*.") The procedure commonly employed is to remove the worm with a hooked needle when it is migrating through the corneal conjunctiva. This requires considerable skill and must be carried out speedily, else the worm will have wandered elsewhere into a less accessible hiding place. Ligation of the worm facilitates its removal with minimal damage to the cornea. Elliot (1918) advises that cocainization of the eye often disturbs the worm, so that it rapidly abandons the conjunctiva.

... bites of the fly in infected areas and anti-*Chrysops* campaigns. Fly repellants as benzyl benzoate and dimethyl phthalate, applied to the exposed skin, will keep off the flies for periods of a few hours, but are not practical for exposed native populations.

Two unfertilized female worms, one removed in two parts from under the conjunctiva and one from the neck of a European woman in India, have been tentatively referred to the genus *Loa* under the name *Loa inquirenda.* The worms had been felt three years previously under the skin on the front of the patient's thigh, but the lesion was regarded as a swollen lymphatic by the physician who was consulted. There was a 6 per cent eosinophilia. The worms contained neither immature eggs nor microfilariæ and 15 thick blood films, taken at various hours were microfilaria-free. It is believed that the worms were mature but sterile, due to the probable absence of males. The two portions of the worm removed from the conjunctiva were 30 mm. and 55 to 60 mm. long but were badly damaged and partly eviscerated. That removed from the neck was 13 to 14 cm. long by 0.6 to 0 64 mm. in diameter. Maplestone (1938) states that these worms are clearly not *Wuchereria bancrofti* and most closely resemble *Loa loa* "because of the shape of the anterior end, the short esophagus, the position of the vulva and the cuticular bosses." They differ, however, in being two to three times as long, in having a straight caudal extremity and a subterminal anal pore.

FILARIOID NEMATODES INADEQUATELY DESCRIBED, RARE OR OF UNCERTAIN IDENTIFICATION

The following list of mature, immature and microfilarial stages of filaria worms is included for reference. Some of these are probably good species but have been inadequately described; others are possibly immature stages of well known species; still others may be purely fictitious. The names "*Filaria*," "*Agamofilaria*" and "*Microfilaria*," as used in this group, are of little or no generic value but are used in the older group sense to indicate that they are filarioid nematodes.

Filaria conjunctivæ Addario, 1885. (*Vide supra* under *Dirofilaria* [*Nochtiella*] *conjunctivæ.*)

Filaria extraocularis Skrjabin, 1917 (= *Dirofilaria conjunctivæ* ?).—(**Synonym:** *Loa extraocularis* Skrjabin, 1917.) This form is known *only from* an immature female obtained from a small tumor of the orbital cavity of a peasant in the Caucasus. The worm measured 14 8 cm. in length by 0.612 mm. in breadth, possessed a finely-striated cuticula, esophagus 935 μ by 85 μ, nerve ring 272 μ from the anterior extremity, anal opening 100 μ from the caudal end and vulva 2 4 mm from the head ... This form has been obtained only once, ...

the rounded ends. The cuticula was smooth. The mouth was encircled by ... of two small lateral, and four submedian papillæ. The anus was subterminal.

Agamofilaria oculi v Siebold, 1839.—(**Synonyms.** *F. oculi humani* v. Nordmann,

1832, *F. lentis* Diesing, 1851.)—Specimens of this worm have been reported three times from the crystalline lens of man but the descriptions are inadequate to state whether the worms even belong to the Filarioidea.

Filaria taniguchii Penel, 1904.—(**Synonym** *F. bancrofti* Taniguchi 1903, *nec* Cobbold,
0 2 mm.
groin of a
geneous and the cuticula finely striated. The mouth was provided with lips, consisting of four lobes, each bearing 2 pairs of very small papillæ. There were no teeth or other armature. The vulva was situated 1.3 mm. from the anterior end. The anal pore was very inconspicuous and was located 0.23 mm. from the caudal ex-
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ien elongated,
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medan policeman in Bombay had a nocturnal periodicity, was "unsheathed," and had a truncated tail. It measured 131 μ by 5 3 μ. It may have been a small or shrunken type of *Mf. bancrofti*.

Microfilaria romanorum Verdun, 1907.—(**Synonym:** *Mf romanorum-orientalis* Sarcani, 1888.)—This microfilaria, described as 1 mm. in length, from the blood of a Roumanian, is a very dubious species entity.

Filaria sp. Parodi and Bonavia, 1920 (=*Dirofilaria conjunctivæ* ?).—This form, described from a single adult female specimen, was extracted from the eye of a woman of French origin in Argentina The worm measured 110 mm. in length by 0 41 mm. in diameter, had a whitish, finely-striated cuticula, an unarmed mouth and a vulva situated 0.5 mm from the cephalic end. The embryos *in utero* were "ensheathed," and measured 250 μ by 6 μ No microfilariæ were found in the conjunctiva, where the parent worm moved about freely. It seems altogether improbable that this is the adult form of *Microfilaria tucumana* Biglieri and Aráoz, 1917, obtained from peripheral blood of patients in North Argentina. (See *Mansonella ozzardi*, p 536)

Filaria sp. Dumas and Pettit, 1919.—A single male specimen of this form was obtained from the scrotal wall of a French railway employee suffering from hydrocele of the scrotum. Brumpt (1922) believes it to be a parasite of some other host, accidentally developed in man.

Suborder Camallanina (Chitwood, 1937) Pearse, 1936

Members of this suborder have a mouth usually lacking pseudolabia but at times formed by two lateral "jaws." The esophageal glands are usually uninucleate

SUPERFAMILY DRACUNCULOIDEA CAMERON, 1934

Members of this superfamily have a mouth which is a simple pore, surrounded by an inner circle of 4 to 6 papillæ and an outer circle of 4 double papillæ, and with the amphids posterior to the lateral papillæ. The esophagus and intestine are vestigial. The vulva, which is situated ventrally near the female worm's equator, atrophies before the worm

becomes sexually mature. The uteri are divergent. The larvæ discharged from the gravid females are "rhabditoid." Of the two recognized families, **Dracunculidæ** Leiper, 1912, and **Philometridæ** Baylis and Daubney, 1926, a human representative is found in the former family.

Type Family DRACUNCULIDÆ Leiper, 1912

(*Synonym:* Fuelleborniidæ Faust, 1929)

This family of nematodes contains species in which the female worm is enormously longer than the male. The posterior end of the male is conspicuously coiled ventrad. The copulatory spicules are unequal or subequal. Several pairs of perianal papillæ are always present. In the gravid females the uteri come to fill practically the entire body, the vulva becomes atrophied and the vagina disintegrated, and the larvæ are discharged by prolapse of the uteri from a rupture of the body-wall near the mouth. The anus is also non-functional in gravid f... ... females are viviparous, ... "rhabditoid" larvæ. ... fresh-water copepods, which, when swallowed in raw water, convey the infection to the definitive host, in which the worms mature in the viscera or subcutaneous tissues. The classical representative of the family, *Dracunculus medinensis*, is an important human parasite.

GENUS DRACUNCULUS REICHARD, 1759 EMEND. BRACKETT, 1938

(*genus from draco*, dragon, serpent)

Dracunculus medinensis (Linnæus, 1758) Gallandant, 1773. (The *Medina worm*, Guinea worm, serpent worm or dragon worm, producing dracunculosis, dracunculiasis or dracontiasis.)

Synonyms.—*Gordius medinensis* Linnæus, 1758 (*vel.* 1785); (?) *Vena medinensis* (Linn., 1758) Gallandant, 1773; *Dracunculus oræcorum* Gruner, 1777; *Filaria medinensis* ... *ena medinensis* (Linn., 1758) Modeer, 17... 3; *Dracunculus æthiopicus* (Val., 1856) Schne... Dunglison, 1895; *Fuelleborinius medinensis* (Linnæus, 1758) Leiper, 1926.

bad and parts ... introduction, ... the Guianas a ...

found that dracunculosis became extinguished in Bahia States, Brazil as the result of a particularly dry season which dried up the ponds in which the intermediate host, *Macrocyclops fuscus* lived. Autochthonous human cases have also been reported from the Netherlands Indies. In North America it has been reported from

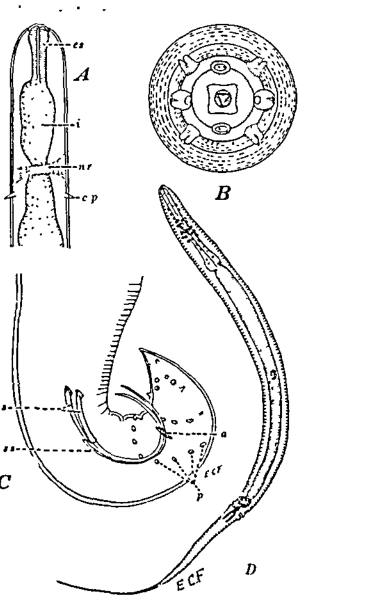

Fig. 280. *Dracunculus medinensis*. *A*, anterior end of female, ventral view, showing cephalic tip, cervical papillae (*cp*), esophagus (*es*), esophageal gland (*i*) and nerve ring (*nr*). *B*, head-end view of worm. *C*, posterior end of male, ventrolateral aspect, showing anus (*a*), copulatory spicules (*cs*), distribution of pre-anal and post-anal papillae (*p*), and spicular sheath (*ss*). *D*, larva of the dracunculus as discharged from the parent worm, with esophagus, mid-intestine, anal opening and anal papillae, nerve ring and genital primordium. *A*, × 60; *B*, × 250; *C*, × 75; *D*, × 200. (Original adaptations *A*-*C*, from Moorthy.)

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Structure of the Adult Worms.—The adult worms develop in the viscera or in the subcutaneous connective tissue. The gravid females measure from 70 to 120 cm. in length (with an average somewhat under a meter) by 0.9 to 1.7 mm. in diameter. Until the recent investigations of Moorthy (1937) male worms had been definitely reported on only two occasions, a single mature worm measuring 40 mm. in a natural infection from India, and two immature worms from an experimental infection in the monkey (Leiper's case), with a length of 22 mm. Moorthy's 45 males obtained from experimentally infected dogs, ranged in length from 12 to 29 mm. and had a maximum diameter of 0.4 mm. The worms are elongate, cylindrical threads or cords, bluntly rounded at the anterior extremity and recurved ventrad at the caudal end, which serves as an anchor for the worms. The cuticula is smooth. The anterior end (Fig. 280 *A*, *B*) has a cephalic prominence. The minute triangular mouth lies in an oval or quadrate prominence and is surrounded by an inner circle of 6 well-developed papillæ, of which the two laterals are single, but the two ventrals, and at times the two dorsals, may be partly fused to form a twinned pair (Fig. 280 *B*). The amphids are just exterior to, and in a transverse plane posterior to the interno-lateral papillæ. A pair of lateral cervical deirids is found just behind the plane of the nerve ring, only 1 mm. from the anterior end. The mouth opens directly into the short, narrow, muscular esophagus, which merges with the distended glandular esophagus some distance in front of the nerve ring, which produces a marked constriction in it. The glandular portion of the esophagus proceeds some distance backwards (from a few to 40–60 mm., depending on the length and sex of the worm) before it is continued as the long cylindrical mid-intestine, which empties *via* a short conical rectum, and opens through a minute anal aperture, a short distance from the caudal extremity (0.25 mm. in males and small females, 0.9 mm. or more in mature females). The posterior end of the male (Fig. 280 *C*) is coiled on itself one or more times. The genital papillæ (*p*) consist of 10 pairs, of which 4 pairs are pre-anal and 6 pairs post-anal. · subequal, measuring 490 to 730 μ long. · ' 200 μ.

The caudal end o' . . 'our minute tips but these are lacking in the mature females The vulva is situated about 10.3 mm. from the anterior end of the worm.

As the female becomes sexually mature, she migrates to a position under the skin in an area of the body which is frequently or periodically bathed in water. When the cephalic end of her body approaches the skin layer, it produces a small, papular induration and vesiculation of the dermis. Such papules are most frequently found on the extremities of the body, but may develop on the abdomen or back. Within twenty-four hours each papule has developed into a blister, which may soon rupture or may increase

in size for four or five days. Sooner or later, however, it breaks open near the center. If the infected member then comes in contact with fresh water, a delicate loop of uterus, which has prolapsed through a ruptured part of the worm's body near the head, will be extruded, will burst open and discharge motile larvæ into the water. Successive discharges of larvæ will typically occur whenever the head of the ulcer comes in contact with water, until the entire progeny have been evacuated.

Life Cycle.—The rhabditoid larvæ which are set free into the water (Fig. 280 *D*) are wiry objects, measuring 500 to 750 μ in length by 15 to 25 μ in greatest diameter, with a bluntly rounded anterior end and a long, attenuate caudal process. Esophagus, mid-intestine, anal pore, nerve ring, and genital primordium may be recognized, as well as a pair of anal papillæ set into deep pockets, one on either side of the anal opening. The cuticula is conspicuously marked with transverse striations. The larva moves about with a stiff motion, at times coiling on itself to form a Greek letter "α" It has no boring apparatus, or other means of gaining active entrance into the intermediate host. If, however, specimens of an appropriate species of *Cyclops* are present in the water, a condition which is frequently fulfilled in endemic areas, some of the larvæ are ingested by the *Cyclops* and, on reaching its mid-intestine, break through the soft wall and come to lie in the celomic cavity of these animals. More than five or six of the larvæ usually cause the death of the Cyclops. In suitable species of Cyclops [*C. quadricornis* auct., syn., *C. strenuus pro parte*, *C. viridis pro parte; C. strenuus*, *C. viridis*, *C. bicuspidatus*, *C. magnus*, *C. vernalis*, *Eucyclops agilis* (= *C. serrulatus* auct), *Macrocyclops fuscus* (= *C. coronatus* ... *ternis* (?), possibly *Thermocyclops hyalin*... *cyclops varicans*, *M. linjanticus*, and other species], the larvæ proceed to undergo metamorphosis, with a loss of the striated cuticula about the eighth day and two days later the development of a delicate enveloping sheath Subsequently they become quiescent and show no inclination to quit the Cyclops. If, however, after metamorphosis of the larvæ, the Cyclops with their parasitic progeny are accidentally ingested by man in raw water, the action of the gastric juice causes the larvæ to be active again, they escape from the semidigested Cyclops body, penetrate the wall of the digestive tract (whether the stomach or duodenal wall, is not clear), and migrate through the tissues, coming to lodge in the viscera or subcutaneous connective tissue, where a period of not less than eight months is required before the female worms are mature and are ready to migrate to the skin to discharge their young.

In addition to the human host, dracunculus worms have been reported from dogs, horses, cattle, leopards, polecats, monkeys, baboons, and the cobra (?) from the Old World, and from the fox, silver fox, raccoon and mink in North America. Leiper (1907) was successful in infecting a monkey by feeding Cyclops containing mature *Dracunculus* larvæ, but Fairley and Liston (1925) failed to infect *Silenus sinicus*. Dogs have been successfully infected on several occasions (Hsu, 1933, Moorthy, 1937). It is in dogs that males were first developed in numbers (Moorthy, *l. c.*).

Epidemiology.—Man becomes infected from ingesting infected *Cyclops* in raw drinking water. In India and probably in other countries where religious ablutions require rinsing of the mouth at the time the body is "purified" by water, infection is most frequently acquired during this ceremony. The water has previously been contaminated by infected persons who have waded into the water, thus allowing the larvæ to escape from cutaneous lesions.

In 1946 Lindberg reported on a two-year survey for dracunculosis conducted in Bhosra, a Deccan village of India. He found that there was a much higher incidence among those drinking from step wells than from curb wells (viz., 38.0 vs. 14.5 per cent); that the rate was significantly higher in males than in females of both categories, that the incidence rises steeply from four years of age to 85.6 per cent in the thirty to thirty-five year quinquennium, then decreases rapidly. The number of worms varied from 1 to 50, although few patients had more than 6. One individual had fifteen worms in a single year. In Jodhpur (Rajputana State, India), which is in a highly endemic area, Lindberg (second communication, 1946) found 1 to 3 per cent of the hospital attendants infected. Since well water is often brackish, the population depend primarily on rainwater for drinking. The high incidence of onsets extends from May to September (Monsoon rainy season), with the peak in July, the warmest month, when the larvæ incubate most rapidly in *Mesocyclops leuckarti*, the proven intermediate host of the area.

Pathogenesis, Pathology and Symptomatology.—Of the many clinical studies on Medina-worm infection Fairley and Liston (1925) were the first to investigate this phase of the subject adequately. From an analysis of 140 cases these workers showed that the incubation period (eight to twelve months) is essentially symptomless, and that the onset of symptoms occurs just a few hours preceding localized manifestations of the infection under the skin, due to the migration of the gravid female from the deeper tissues to a cutaneous site. The prodromal symptoms consist of erythema and

to toxic secretions of the worm which have been absorbed into the system.

The local lesions become evident a few hours after the onset of the

on the amount of exudation underneath the blister and the length of time before the blister ruptures. They are most commonly situated on the lower extremities, but may occur on the upper extremities, the trunk, buttocks, and scrotum. Lindberg (1946) found the sites of emergence among infected individuals in Bhosra village, India to be as follows: foot, 112; ankle, 248; leg, 245; knee, 60; thigh, 50; hip, 11; hand, 5; wrist, 5; forearm, 6, elbow, 2; shoulder, 1, chest, 4; abdomen, 2, and scrotum, 6. Not infrequently they occur on the sole of the foot or between the metatarsal bones (Fig. 281).

The fluid from the cavity of an unruptured lesion is a yellow serum, which

is invariably sterile on culture. It usually contains large numbers of mononuclear cells, eosinophils and polymorphonuclear leukocytes, as well as larvæ of *D. medinensis.* The lesion at the moment of spontaneous rupture consists of an outer layer of skin which forms the dome, a concave partly necrosed base, and an intermediate septum of fibro-gelatinous material, the intervening spaces being filled with a fluid exudate (Fairley's "blister fluid"). Near the center of the base is a pore, communicating with an adventitious tunnel, in which the female worm is found. The head of the worm at the time of vesicle formation is usually just beneath the base of the lesion or actually protruding into the cavity of the vesicle.

FIG 281 —Dracunculus worm partially removed from a ruptured eschar of the fourth toe (After Castellani and Chalmers, Tropical Medicine)

The rupture of the vesicle relieves toxic symptoms but is usually the occasion for the introduction of pyogenic organisms, which not only invade the cavity of the superficial lesion but travel up the tunnel and thus greatly aggravate the condition These complications are frequently more serious than the original infection. Sequelæ of this infection include arthritis,

ith the

living

in an endemic area and of previous infection provides substantial presumption of infection. The method utilized by the female worm in effecting a discharge of the larvæ, as well as the type of larvæ set free, are unique and constitute a specific diagnosis. Ramsay (1935) obtained 85 per cent accurate diagnoses with 0.25 cc. of a 0.25 per cent physiological salt solution extract of *Dracunculus* antigen used intradermally in 41 positive cases of dracunculosis in Nigeria. This worker states, however, that the reaction may remain positive years after the infection has been terminated. Old calcified worms may be diagnosed by x-rays.

Therapeusis.—The systemic symptoms which precede local vesicle formation completely disappear upon administration of epinephrin. Gore (1938) has reported that ichthyol compresses, placed on the skin over the track of these worms, reduce the [illegible]

O [illegible] of [illegible] and Liston (*l. c.*) proposed an operative technic, by incising the tissues in three or four places overlying the tunnel and withdrawing the worm in parts, care being taken not to draw the portion of the worm which has come in contact with the outer septic crater back into the tunnel. In endemic countries the *Dracunculus*-infected natives roll the worm out inch-by-inch as it emerges from the patent lesion.

In 1942 Elliott reported on his success in removing *Dracunculus* with a *phenothiazine* emulsion, in 23 of 59 patients who came under his observation in a British military hospital in West Africa. The emulsion was prepared as follows: (1) 2 Gm. of finely powdered phenothiazine were mixed with 0.35 Gm. lanolin and 15 cc. sterile olive oil, previously heated at 150° C for one hour; (2) 5 cc. sterile distilled water were added to make the emulsion; (3) an additional amount of 20 cc. sterile olive oil was then introduced; (4) the emulsion was poured into 60 cc. (2 oz.) bottles and autoclaved at 115° C. for 30 minutes. The linear area to be injected was first anesthetized with novocaine, then 20 cc. of the well-shaken emulsion injected intramuscularly into the central path of the worm, followed by 10 cc. on either side. The region was then massaged briskly for five minutes. After five to seven days the worm may be withdrawn by careful traction, preceded by manual pressure on the track of the worm, working from the inner end towards the opening of the sinus.

Prognosis.—Even with the almost constant opportunities for pyogenic infection of the tunnels in natives who possess no knowledge of personal hygiene, prognosis is good, unless septicemia supervenes.

Control.—Epidemiological evidence in India points to pools, draw-wells and step-wells as being the places of infection with *Dracunculus*. On the West Coast of Africa the village ponds are believed to be the most likely source of infection. In both regions, however, the actual conditions for propagating the infection are essentially the same, namely, (1) the periodic, or at times daily contact of the body of infected individuals, discharging viable larvæ, with water, (2) which harbors appropriate species of Cyclops, and (3) the use of this raw infested water for drinking purposes or to rinse out the mouth for purposes of ablution. By confining the water for drinking purposes within a cemented curb, so that the legs of the water-carriers do not come in contact with the household supply and so that the water spilled over the curb cannot flow back into the well, the infection in certain endemic foci can be greatly reduced. It is possible, also, that the water may be treated with chemicals in amounts sufficient to kill the Cyclops and yet leave it potable. Moorthy and Sweet (1936) suggested that certain copepod-feeding small fishes be introduced into infected waters to control the vicious cycle at this point. In most infected countries the natives consider dracunculosis a Heaven-sent curse and look forward to reinfection at least once a year with considerable equanimity.

SECTION V

THE NEMATOMORPHA

CHAPTER XXX

INTRODUCTION

PHYLUM NEMATOMORPHA (VEJDOVSKY, 1886) EMEND. POTTS, 1908, RITCHIE, 1915, PEARSE, 1936

THE members of this phylum are roundworms (*sensu lato*), which as adults have a degenerate intestinal tract; the body cavity is lined wholly or in part with mesothelium; a proboscis is lacking except in the first larval stage. There are two recognized class groups, the **Nectonematoidea** Rauther, 1930 and the **Gordiacea** von Siebold, 1848. The species of medical interest belong to the

Class Gordiacea v. Siebold, 1848 (fide Carus, 1863)

(Synonym, Gordididea Ortlepp, 1924)

Nematomorpha in which the body cavity is lined by mesothelium; gonads not continuous with their ducts, the eggs being discharged into the body cavity and then passed into the ducts; alimentary canal atrophied in sexually mature worms; lateral longitudinal cords wanting; cloaca present in female These are the "hairworms," commonly found as adults in bodies of fresh-water, with larval stage in insects; their presence in the digestive tract of man is accidental.

THE GORDIACEA, OR "HAIRWORMS"

General Biological and Morphological Data.—The worms of the Phylum **Nematomorpha**, Class **Gordiacea**, are familiarly referred to as "hair snakes" or "horse-hair worms," due to the popular belief that they develop from horse hairs which have fallen into drinking troughs, quiet pools, springs or ponds. They are elongate objects, buff to dark brown in color, and densely opaque. Their movements are stiff and wiry, and, at times, spring-like. They are interesting biologically in that the immature larval stage is parasitic in various insects, while the adults are characteristically free-living. It is the adult stage which has been reported from time to time as "parasitic" in the human intestinal tract.

The adult free-living worms are diecious. They are elongate capillary nematodes, varying in length from 10 to 50 cm. The anterior ends are more or less bluntly rounded; the posterior end of the male is bifurcated behind the anus or at least possesses a *dorsoventral groove*, while that of the female is either entire or trilobate. There are no lateral lines. The somatic layers consist of a relatively thin outer cuticula, a thicker inner cuticular layer with obliquely crossed fibers, a hypodermis with numerous *nuclei, glandular and nerve elements and a very thick muscular layer.*

Internally the body cavity is at first filled with a ...

... present in both sexes. Furthermore, the males lack an accessory genital apparatus.

The sexually mature worms mate in the water, where the eggs are laid in strings. When fully developed, the larvæ rupture the egg membrane and escape by means of a beak-like proboscis, provided with retractile

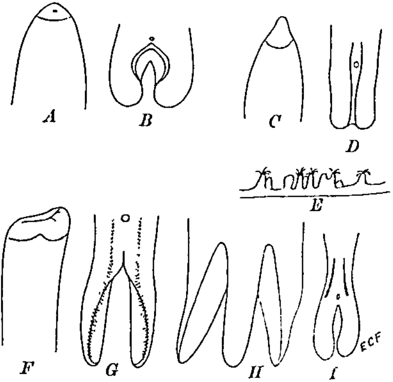

FIG 282 —Characteristics of Gordiacea *A*, anterior extremity, and *B*, posterior extremity of ...

Torino, Italy)

stylets and with three rows of large reversed spines. These larvæ bore their way into any animal tissue which is near at hand. In case they penetrate the body of various Orthoptera and other insects, they first enter the adipose tissue, but later migrate to the hemocele of the host, where

The Class **Gordiacea** v. Siebold, 1848 is composed of two families, **Gordiidæ** Diesing and **Chordodidæ** May.

Family I. GORDIIDÆ Diesing, emend. H G. May, 1920

The species of this family have a smooth cuticula, without true areoles; the body bristles are derived from the fibrous cuticula The buccal cavity, when present, is not connected with the intestine. The ovaries are not connected or enclosed by mesenchyme. The posterior end of the male is provided with two projecting lobes or prongs arising behind the anus. A ... The caudal end of the female is entire The

... "parasites" of man: ... and one from El S... *G setiger* Schneider, 1866 (syn *G. villoti* Rosa, 1882), 3 cases from Europe; and *G. chilensis* E. Blanchard, 1849, 1 case from Chile, S. America, and *Gordius* sp. (probably *G. robustus*) from Florida and from S. Carolina (U. S. A.).

Family II. CHORDODIDÆ May, 1920

The species of this family have a rough cuticula, with true areoles; the tubercles and body bristles arise from the non-fibrous cuticula. The ovaries are enclosed by mesenchyme, giving the appearance of a "double mesentery." The posterior end of the males is forked or provided with a dorsoventral groove, but they have no post-anal crescent The caudal end of the female is either entire or provided with three lobes. The larvæ of this family have a short body which is posteriorly rounded and provided with postero-lateral spines. There are ten recognized genera which belong to this family (Carvallo, 1942), viz., *Chordodes* Creplin, 1847 (Fig. 282 *C, D, E*), *Paragordius* Camerano, 1897 (Fig. 282 *F, G, H*), *Parachordodes* Camerano, 1897 (Fig. 282 *I*), *Euchordodes* Heinze, 1937, *Chordodiolus* Heinze, 1935, *Gordionus* Muller, 1927, *Beatogordius* Heinze, 1935, *Paragordionus* Heinze, 1935, *Neochordodes* Carvallo, 1942 and *Pseudochordodes* Carvallo, 1942. The following species of this group have been reported as "parasites" of man: *Chordodes capensis* Camerano, 1895, 1 case from British East Africa, *Paragordius tricuspidatus* (Dufour, 1828), 1 case from France; *P. varius* (Leidy, 1851), 6 cases from North America; *P. cinctus* v. Linstow, 1906, 1 case from the Transvaal, S. Africa; *P. areolatus* v. Linstow, 1906, 1 case from S. E. Africa; *P. esavianus*, one case from Brazil; *Parachordodes tolosanus* (Dujardin, 1842), 2 cases from France, 2 from Italy, *P. violaceus* (Baird, 1853), 1 case from France; *P. pustulosus* (Baird, 1853), 1 case from Italy; *P. alpestris* (Villot, 1884), 1 case from France; and *P. raphaelis*, one case from South Africa.

The "Parasitism" of Gordiacean Worms in Man.—The earlier writers ...

... human digestive tract. Present information regarding the life cycle of this group suggests that the adults, or rarely the adolescents, of these species enter the body accidentally in raw drinking water or in their insect hosts They may remain undigested for some little while in the digestive tract,

during which time their movements and possibly their secretions may occasion mild intestinal disturbances. They may be passed alive *per anum* or vomited. In two instances (*Parachordodes raphaëlis* and *Paragordius esavianus*) the worms have been reported as passed *per urethram* by young females, the former in South Africa (Baylis, 1941), the latter in Espirito Santo State, Brazil (Carvallo, 1942). Symptoms believed to have been caused by their presence over long periods of time are probably due to other causes.

However, there is one authentic record of accidental, but nevertheless true, tissue parasitism of a gordiid worm in man (Sayad, Johnson and Faust, 1936). A juvenile female of *Gordius* (probably *G. robustus*) was partly removed and partly left *in situ* in a tumorous tissue pocket, which had developed on the lower border of the orbit of an adult white male patient living in Miami, Florida. The presence of the worm in this site had provoked considerable tissue reaction, with eosinophils, epithelioid and giant cells in the immediate vicinity of the worm.

SECTION VI

THE ANNELIDA

The phylum ANNELIDA contains metazoan invertebrates which have true segmentation (*i. e.*, metamerism), a complete digestive tract, a well-coordinated nervous system, a circulatory system and a body cavity lined with mesothelium. There are six recognized class groups, namely **Archiannelida** Hatschek, 1878; **Polychæta** Grube, 1850; **Oligochæta** Grube, 1850; **Myzostoma** Graff, 1884; **Echiurida** Savigny, 1817, and **Hirudinea** Lamarck, 1818. The only class group of medical importance as parasites of man is the Hirudinea, which, in a broad sense, are included among the Helminths.

CHAPTER XXXI

THE LEECHES (HIRUDINEA)

GENERAL CONSIDERATIONS

The leeches are predatory or parasitic organisms belonging to the Phylum Annelida. They have both an anterior and a posterior sucker, which are used for attachment and also aid materially in their caterpillar-like locomotion. They are regarded as distant relatives of the annelid Family [illegible] suckers, jaws, a [illegible]. However, leeches [illegible] like ticks, have a mechanism adapted for the engorgement of relatively large amounts of blood. They vary in size from small macroscopic, vermiform objects to those many inches in length, they vary in shape from elongated cylindrical or ovoidal to broadly ovoidal or pyriform bodies. They are dorsoventrally compressed; the dorsal side is convex and the ventral side flattened or concave. Some leeches are aquatic, others terrestrial, and still others amphibious in their habits.

Segmentation (*i. e.*, *metamerism*) in the leech is much more complicated than it is in most of the oligochetes In the leech the external annulation does not correspond to the internal metameres or somites, since each true metamere is provided with a few to many external rings or annulations. Most investigators agree that there is a maximum of 34 somites in the leech's body, distinguished by a similar number of ganglia in the central nervous system and a similar number of rows of sensory papillæ. Externally there may be from two to sixteen annulations for each somite. The ganglion lies in the median annulus of each metamere. Near the equator of the body there is the full number of annulations characteristic for the genus or species but at the anterior and posterior extremities the number is reduced.

STRUCTURE AND LIFE CYCLE OF LEECHES

The body is covered with a thin, smooth *cuticula*, which is from time to time cast off in patches. Immediately beneath is the *epidermis*, consisting

of wedge-shaped cells which are internally separated from one another by blood capillaries. From the epidermis are produced many unicellular glands, disposed in the underlying connective tissue but opening to the surface through long ducts. There are special glands, usually situated in the ninth, tenth and eleventh metameres (*clitellar somites*) which secrete the cocoon-forming material.

In addition to th [illegible]

[illegible] of each metamere. These papillæ are usually more numerous on the dorsal than on the ventral aspect of [illegible] e ventral surface of metameres 7 to 23, on [illegible] t of the median annulus of each metamere, a [illegible] the *nephridiopores*. On the dorsum of each of the first five metameres in most leeches there is a pair of *eye-spots*, which are modified sensory papillæ, but in some species the number of eye-spots is reduced. Except for the genus *Acanthobdella* leeches bear no setæ. A few species possess external gills or *branchiæ*.

Leeches may be leukodermatous or they may be provided with brown, black or other pigments so distributed as to form longitudinal stripings or ornate, bilaterally symmetrical patterns. Moreover, the lateral pouches of the digestive tract, when distended with blood, may provide a beautifully patterned picture which is visible from the surface of the worm.

The leech is quite muscular, due to an outer layer of *circular muscles* next to the epidermis, an underlying, much thicker layer of *longitudinal muscles, dorso-ventral fibers* and *radial fibers*. Internal to the two main muscular layers is the so-called *botryoidal tissue*, which consists of branched lacunæ surrounding the digestive tract. The walls of these lacunæ or canals consist of large cells loaded with black pigment. The botryoidal tissue communicates both with the blood-vascular system and the greatly reduced body cavity. All of the unoccupied interstices between the epidermis and the digestive tract are filled with *connective tissue*, consisting of cells and fibers in a gelatinous matrix.

The Digestive System.—In one order of leeches (the Rhynchobdellida) the oral end is provided with a protusile proboscis; in another order (the Gnathobdellida) there is no proboscis but a group of three very muscular *jaws* (Fig. 283, *A*), one medio-dorsal and two ventro-lateral in position within the oral sucker. Each jaw is like a hard cushion, is covered with chitin and is frequently provided with numerous serrated denticles. By means of powerful muscles these three jaws operate to produce the characteristic triradiate wound in the victim's skin. (See Fig. 283.) The small mouth cavity leads into the very muscular *pharynx* (*ph*) (somites 4–8), surrounding which are numerous unicellular *salivary glands*. These latter open near the mouth cavity and serve to secrete an anticoagulin which prevents the clotting of ingested blood. The pharynx communicates distally with the extensive, thin-walled *crop*, which extends from the levels of the eighth to the eighteenth somite and has 11 pairs of pouches or diverticula (*di*). The crop is the portion of the digestive tract which is capable of tremendous distention when the leech takes a full blood meal. In it a portion of the blood meal may be stored for many months. Immediately

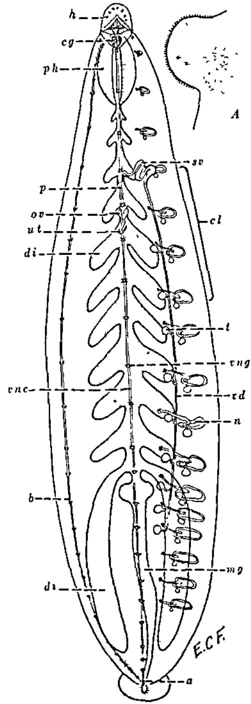

FIG. 283.—Diagrammatic representation of the medicinal leech, *Hirudo medicinalis.* Only one member of the pairs of lateral blood-vessels, nephridia and male genitalia is shown. *a*, anus, *b*, lateral blood-vessels; *cg*, cephalic ganglion or 'brain', *cl*, clitellar somites, *di*, diverticulum of crop; *h*, "head," with eye-spots, *mg*, mid-gut; *n*, nephridium, *ov*, ovary; *p*, penis, *ph*, pharynx, *sv*, seminal vesicle, *t*, testis, *ut*, uterus; *vd*, vas deferens, *vnc*, ventral nerve cord, *vng*, ventral nerve ganglion. × 2 *A*, detail of one of the three hammerhead jaws with marginal denticles, greatly enlarged. (Original adaptations.)

behind the crop is the tubular stomach or *mid-gut* (*mg*), in which digestion takes place. Its anterior end is dilated and the wall of its distal portion is spirally infolded. When blood passes from the crop to the stomach, its color changes from reddish-brown to green. Behind the stomach is the short *intestine*, which, in turn, leads into a short *rectum* and opens externally through a small *anal pore* (*a*), anterior and dorsal to the posterior sucker.

The Excretory System.—This consists of 17 pairs of *nephridia* (*n*) situated in segments 7–23. In general, these nephridia are like those of the earthworm, but they are more complex and variable. Each nephridium consists of (*i*) a sinuously looped glandular tubule, with a ciliated inner funnel, which is at times occluded; (*ii*) a central duct running through the cells of the tubule and many branched communicating ductules; (*iii*) a dilated vesicle at the outer end of the primary duct, and (*iv*) a terminal nephridiopore which opens on the ventral surface of the worm.

The Blood-vascular System.—There is a distinct vascular system, consisting of (*i*) *blood-vessels* with muscular walls and (*ii*) *blood sinuses* without muscular walls. The former consist of a pair of lateral trunks (*b*), which unite at the anterior and posterior ends of the worm and also send off metameric dorsal and ventral branches, some of which anastomose with one another. The terminal branch vessels end in capillaries in the cuticula, nephridia, gonads, etc. The blood sinuses, which represent a greatly reduced body cavity, consist of a dorsal and a ventral trunk. These also have anterior and posterior connections, and metameric branches, ending in terminal capillaries which constitute their only communication with the blood-vessels The circulating blood consists of plasma, at times colored with hemoglobin, and a small number of colorless corpuscles.

The Nervous System.—The central nervous system consists of a series of partially fused paired ganglia (*vng*) united by twinned nerve cords (*vnc*), which lie within the ventral blood sinus. At the anterior end of the system there is a conspicuously large cephalic or subesophageal ganglion (*cg*) (representing five fused pairs), which is united by circumesophageal commissures with the small dorsally situated brain. This latter lies above the anterior end of the pharynx. Nerves arising from the ganglia innervate the more important organs and tissues of the body, including the pairs of eye-spots on the dorsal side of the anteriormost metameres, the metameric sensory papillæ, the suckers, genitalia, etc.

The Reprod[illegible]

possesses 1 to [illegible]

vas efferens, an [illegible]

(*vd*), which continue as paired *seminal vesicles* (*sv*), each being usually provided with a *prostate* gland, an *ejaculatory duct* and a muscular *penis* (*p*). The two ejaculatory ducts enter a common *bursa copulatrix* or *genital atrium*. The ovaries (*ov*) consist of a single pair of coiled, filamentous sacs which are continuous with their ducts. The two ducts unite to form a common convoluted *oviduct*, which is continued as a muscular *uterus* (*ut*) and opens through a short vaginal tube in the mid-ventral line, one metamere behind the male genital opening (usually stated to open on somite 9).

Reproduction and Life Cycle.—In some leeches insemination is accomplished when one leech implants onto the cuticula of another a horny

pocket or *spermatophore*, from which spermatozoa issue forth, migrate through the tissues of the recipient and reach its ovary. In the group to which the medicinal leech (*Hirudo medicinalis*) belongs, reciprocal copulation takes place by the introduction of the penis of each into the vagina of the other and the reciprocal deposition of a spermatophore. Thus, in either type, fertilization takes place before the eggs are laid. Some species of aquatic leeches deposit a few eggs at a time in small tough capsules which are attached to submerged objects. Other leeches surround their eggs with a cocoon, which is then deposited in or amongst submerged objects, on the bottoms of lakes and ponds, or in moist earth. The capsule or cocoon is secreted by glands of the clitellum and hardens on contact with water. Species of still another group carry both their eggs and their young around with them. As soon as the leechling is able to suck blood, it leaves the parent and takes up an independent existence.

CLASSIFICATION OF LEECHES

The leeches are divided into three orders, the *Gnathobdellida* Vaillant, 1890, the *Rhynchobdellida* Blanchard, 1897, and the *Pharyngobdellida* Johansson, 1913. Forms of special medical importance are found in the

GNATHOBDELLIDA Vaillant, 1890.

This group contains species having a smooth cuticula, a mouth lacking a proboscis but usually armed with three jaws or pseudojaws, frequently armed with denticles, and a spoon-like anterior sucker.

MEDICAL IMPORTANCE OF LEECHES

Throughout the years leeches have been regarded as having a two-fold medical importance, namely (1) as a medical aid and (2) as detrimental or dangerous predators of man.

Leeches as a Medical Aid.—From the time of early Greek medicine there are records of the use of leeches for blood-letting, a practice commonly employed by physicians until the middle of the nineteenth century. During the Middle Ages and even until quite recently the so-called "medicinal leech" (*Hirudo medicinalis* or a closely related species) has been employed in Europe and America for the partial exsanguination of patients suffering from every variety of ailment from common colds to cancer. The use of leeches was so universally accepted as a part of medical art that by analogy the physician him*self* was referred to as a *leech*. So great was the demand for leeches for medicinal use that suitable species were cultured by the tens of thousands in Europe and the United States. Nachtrieb (1912) states that, about 1850, one American leech farm disposed of as many as 1000 or more leeches daily, and that about seven million were used in London hospitals and five to six million in Paris hospitals in 1863.

With the gradual recognition that in most cases blood-letting was harmful rather than helpful to the patient, the use of the leech as a medical aid has been almost completely abandoned. Moreover, it is generally accepted that the effective anticoagulating principle from the buccal glands of leeches (*i. e.*, *hirudin*) can be applied to a lesion with greater precision and

safety than can the living leech. However, there may be occasional justification for the use of the medicinal leech in certain cases of thrombosis or phlebitis, and possibly in selected types of hypertension without anemia.

Leeches Injurious to Man.—Tourists, as well as natives, who travel through the tropical rain forests of India, Assam, Burma, French Indo-China, Southern China, Ceylon, Indonesia, Celebes, Borneo and New Guinea, or soldiers who march through the humid valleys of the Himalayas or the Chilean Andes, one and all provide colorful accounts of the scourge of blood-thirsty terrestrial leeches that lurk on every stone, leaf and stem, spring onto the wayfarer, painlessly insert their denticled jaws in his skin and produce trickling springs of blood from each puncture site. Moreover, thirsty travelers throughout Northern Africa and Western Asia, as well as natives in parts of Southern Europe, who unwarily lap up water from a spring or brook, may acquire an infestation of the upper digestive or respiratory tract with the aquatic leech, *Limnatis nilotica*, or its close relatives. This subject of leech infestation may be appropriately considered under two categories, depending on whether the injuries produced are external (*external hirudiniasis*) or internal (*internal hirudiniasis*).

External Hirudiniasis.—Although species of aquatic leeches, commonly ectoparasitic on aquatic vertebrates (as fishes, frogs, turtles, molluscs, etc.), will frequently attach themselves to the skin of human beings with whom they come in contact and will avidly suck blood, the leeches which are most notorious in this respect are terrestrial in their habits. These species commonly live in the tropical rain forests, temporarily attached to tree trunks and foliage, to shrubs, grasses or stones, from which they actively spring upon unsuspecting human beings or mammals coming within their reach. More than a dozen species of terrestrial leeches which attack man have been described from Asia, Polynesia, Oceania, Australia, Madagascar and South America. The species which has been commonly encountered and about which there is the largest mass of information is *Hæmadipsa zeylanica*.

H. zeylanica is a relatively small leech, measuring 2 to 3 cm. in length by a maximum of 5 mm. in breadth. It is provided with a powerful oral sucker and three powerful jaws having denticles terminating in very short points. It is found in Ceylon, India, and possibly Malaya, and in certain areas constitutes a veritable scourge to man and beast. In his *Natural History of Ceylon*, Tennent (1860) has provided a classical description of this species: "Of all the plagues which beset the traveler in the rising grounds of Ceylon, the most dreaded are the land leeches (*Haemadipsa ceylonica*). They are not frequent in the plains, which are too hot and dry for them, but amongst the rank vegetation in the lower ranges of the hill country, which is kept damp by frequent showers, they are found in tormenting profusion. . . . Their structure is so flexible that they can insinuate themselves through the meshes of the finest stocking, not only seizing on the feet and ankles, but ascending to the back and throat, and fastening on the tenderest parts of the body. . . . Such is their vigilance and instinct, that, on the approach of a passer-by to a spot which they infest, they may be seen amongst the grass and fallen leaves on the edge of a native path, poised erect, and prepared for their attack on man

and horse. . . Their size is so insignificant, and the wound they make is so skillfully punctured, that both are generally imperceptible and
the first intimation
a chill feeling of the
being distended with
the ground in fury to shake them from their fetlocks, to which they hang in bloody tassels. The bare legs of the palankin bearers and coolies are a favorite resort, and as their hands are too much engaged to be spared to pull them off, the leeches hang like bunches of grapes around their ankles."

Although the puncture is painless, the wounds from which the worms have been removed remain open for a long time and heal slowly, even when not infected with pyogenic organisms. Moreover, uncontrolled bleeding from multiple abandoned sites has been known to produce sufficient exsanguination to cause death in Europeans traveling in infested areas.

The related species in Japan, *H. japonica*, is stated by Whitman to puncture the skin so expertly that its presence is first detected by the trickling of blood from the wound. The species described for the Philippines is *H. talagalla;* that from Java, *H. javanica;* while three species, *H. fallax*, *H. morsitans* and *H. vagans*, have been recorded from Madagascar. Some of the above-named species, or other species, are serious scourges in parts of Sumatra, New Guinea, Celebes, Borneo, French Indo-China, Chile and Trinidad. The land leech of Southern Australia belongs to the genus *Philæmon*.

Internal Hirudiniasis.—This pathological state is due to aquatic leeches accidentally taken into the mouth in drinking water, or gaining entrance to the genito-urinary tract from wading in deep water. Species of several genera of aquatic leeches have been incriminated in internal hirudiniasis,

in length by 1 to 1.5 cm. in greatest breadth. The body is broad posteriorly and more or less pointed anteriorly. The mouth is surrounded by a relatively weak sucker, the upper lip of which has a longitudinal furrow on its inner aspect. The three jaws are armed with a total of more than 100 denticles and are provided with sensory papillæ. The powerful posterior sucker is at least twice as large as the oral one. The dorsum of the body is typically a dark olive green and the venter, dark gray. At times there are dark longitudinal stripes on the dorsum. On each side there is a narrow orange stripe.

L. nilotica lives in quiet brooks, streams, fresh-water ponds and lakes in Southern Europe (Portugal, Spain, France, Italy, Greece, Bulgaria), in Northern Africa (Egypt, Ethiopia, Tunis, Algiers, Morocco), the Azores and the Canary Islands, Western Asia (Turkey, Armenia, Syria, Palestine, Iran, Baluchistan, Seistan, Afghanistan, Chinese Turkestan, and even within the frontiers of India). The species reported from the environs of Singapore is *L. maculosa*, while *L. africana* has been identified from Senegal and the Congo basin, *L. mysomelas* from Senegal and *L. granulosa* from India.

Internal hirudiniasis, produced by undiagnosed species of leeches, has been reported on several occasions from Java and Sumatra. Once an aquatic leech, *Hæmopis cavillina*, was found fixed to the sclerocorneal limbus of an Italian subject (Mazzola, 1929).

The small, young leeches of this species are unsuspectingly taken into the mouth in raw drinking water. During the act of swallowing they frequently become attached to the mucous membrane of the pharynx, nasopharynx, epiglottis, and esophagus. By deep inhalation they may be carried to the larynx or even to the trachea or bronchi. Although their buccal armature is too weak to harm the human skin, they readily puncture mucous surfaces and proceed to engorge themselves with blood. While the medical literature, especially that of rhinolaryngology, contains several [illegible] the majority of the many persons infested each year are relieved by home remedies (gargling with strong salt solution, inhalation of pungent odors and the successful use of a tough twig provided with a single reversed thorn), and that only the most serious cases not amenable to home cures seek the physician. Fewer still consult a specialist. Thus, while the majority of patients probably have a pharyngeal or nasopharyngeal involvement, the literature (*i. e.*, the more difficult cases) reports more than half the patients suffering from infestation of the larynx and vocal cords; 16 per cent, the trachea; 16 per cent, the nasopharynx; 6 per cent, the esophagus, and the remainder, infestation in multiple sites. Witenberg (1944) states that *L. nilotica* is much more likely to be the causal agent of "halzoun" (suffocation) than is the sheep liver fluke (*Fasciola hepatica*). (*Vide supra.*)

Pathology and Symptomatology of Internal Hirudiniasis.—At the site of attachment the leech secretes hirudin, to prevent coagulation of the blood, and proceeds to draw out blood far in excess of its maximum needs. While this blood-letting is almost invariably a painless procedure, the physical obstruction caused by the presence of the worm frequently produces a feeling of pressure, pain, and a nervous uncomfortable sensation emanating from the parasitized focus, together with functional disturbance of the affected [illegible] wound [illegible] mation [illegible]

In case the leech has entered the mouth and has anchored itself to the mucous membrane of the upper respiratory or digestive passage, epistaxis, hemoptysis or hematemesis may result, depending on the organ infested. Prolonged hemorrhage may result in severe anemia, and deaths have been reported from excessive exsanguination (Masterman, 1908). Leeches in the nares may cause a persistent headache. When lodged in the larynx or on the vocal cords, there may be continuous coughing, with a slimy, bloody discharge; there may be pain in the chest, dyspnea with or without cyanosis, hoarseness, and at times complete loss of speech. In the larynx and trachea leeches may produce suffocation, occasionally resulting in death (Manson, 1903). If lodged on the epiglottis or in the esophagus, difficulty in swallowing and nausea are experienced. Messinger (1924) reported leech infestation of a Macedonian woman who gave a history of convulsive coughing

with expulsion of blood for a period of six days. On examination, her pulse was thin and stringy, her lips and nails were blue, her skin pale and her pupils distended. A leech was found attached to an edematous, inflamed vocal cord.

Persons wading or bathing in fresh water at times suffer from leech infestation of the genito-urinary tract. Woolnough (1928) reported uncontrolled hemorrhage from the vagina of a three and one-half year old girl in Australia, caused by leech bite. Hamilton (1933) cites leech infestation of the labium majus which simulated uterine hemorrhage. Several physicians in India, Algeria and Italy have reported leech infestation of the male urethra. One jute washer in India (Ghosh, 1933) observed a leech entering the external meatus of the urethra and was unable to prevent its entry by traction.

In 1903 Kuwahara reported the recovery of 2 to 3 cm. length young specimens of *Limnatis japonica* from the conjunctiva of a patient. The worms have occasioned hemorrhage, photophobia and an excessive flow of tears.

THERAPEUTIC AND PREVENTIVE MEASURES AGAINST LEECHES

External Hirudiniasis.—When fully engorged, the land leech, *Hæmadipsa zeylanica*, drops off. The removal may be hastened by applying a few drops of brine or strong vinegar to the site, or a match flame skillfully applied to the worm. Under no circumstances should the worm be pulled off, lest the jaws be left in the wound and a phagedenic sore develop. If the bleeding from the bites continues for some time, it may be desirable to staunch each wound with a styptic pencil. The wounds should be bathed for several days with mild antiseptic lotions, as boracic acid or calamine, to prevent sepsis.

Persons traveling through areas infested with land leeches should wear knee-length, water-proofed leather boots and closely woven khaki pants.

Insect repellants, such as benzyl benzoate, dimethyl phthalate, Rutgers-612 and Indalone, when applied to the clothing or impregnated into clothing, will provide considerable protection against leeches. Ribbands (1946) found that dimethyl phthalate, when applied to cloth at the rate of 4 cc. per square foot, is completely repellant for land leeches for as long as six days. The most important places for application are the tongue, lace holes and neck of shoes or boots.

Internal Hirudiniasis.—Leeches lodged in the nasal passages may be visualized with a nasal speculum. In the nares, naso-pharynx or upper part of the pharynx they may be cocainized and removed with an appropriate pair of forceps or a probe provided with a sharp hook on its inner end. However, the worm is very slippery and is frequently difficult to grasp. When the worms are situated in the posterior pharynx, larynx, trachea or bronchi, it is desirable to place the patient in the Trendelenburg position before attempting to anesthetize and remove them, in order to prevent the worms from being drawn farther into the respiratory tract by deep inspiration with resultant suffocation. In the more serious cases the use of cocaine is not advised. Through a laryngoscope a long hooked forceps should be used in an attempt to remove the worms by gentle traction. Occasionally

tracheotomy must be resorted to. Should the leech be attached to the wall of the esophagus, visualization and cocainization through an esophagoscope is indicated. When the worm becomes anesthetized, it drops into the

Since the majority of patients suffering with internal hirudiniasis become infested from drinking unfiltered water, it is important that individuals or troops, passing through, or quartered in, regions where *Limnatis nilotica* and its relatives abound, be required to drink only water that has been filtered or at least has been strained through several layers of cheese-cloth. An even sounder dictum, although not always possible of accomplishment, is to boil all suspected water.

SECTION VII

TECHNICAL AIDS IN DIAGNOZIS AND TREATMENT OF HELMINTHIC INFECTIONS

CHAPTER XXXII

THE BASIC EQUIPMENT REQUIRED FOR THE DIAGNOSIS OF HELMINTHIC INFECTIONS

INTRODUCTION

Most laboratories, in which diagnosis is made for helminthic infections, are also expected to carry out parallel diagnosis in bacteriology, serology, urology, hematology and protozoology, and some clinical laboratories are also equipped for pathological diagnosis. Hence, much of the equipment which is suggested in the following pages may be equally serviceable in other lines of clinical diagnosis. However, there are certain sets of apparatus and methods of technic which have been particularly developed to facilitate helminthological diagnosis and without which no all-round laboratory can be developed.

Microscopic Equipment

It is desirable to have at least one compound microscope and one binocular dissecting microscope The compound microscope may be any one of several serviceable models which are on the market It should be compact and capable of hard usage. The fine-adjustment screw should be in a position so that the delicate tension is not strained when the microscope is lifted by the handle There must be at least three objectives, (1) a low-power lens of about 16 mm working distance, (2) a high-power dry lens of about 4 mm. working distance, and (3) a high-power lens of about 1 9 to 2 mm working distance for use with immersion oil It is advisable to have at least two oculars, a medium and a low power For constant microscopic examina-

nose-piece and without altering the focus on a given preparation The advantage of such an arrangement is obvious. the specimen may be examined under binocular

objectives in the best microscopes have either apochromatic or fluorite lenses, but achromatic lenses are satisfactory for routine work The dissecting microscope should be equipped with two or three graded pairs of periplanatic oculars and two or three graded pairs of objectives In case no dissecting microscope is available, a lower magnification and greater working distance of the compound microscope may be obtained by unscrewing the lower portion of the low-power objective, leaving only

a single lens for the objective. It must be remembered, however, that the dissecting microscope gives a direct image while the compound microscope gives an inverted one.

Microscopic equipment will give satisfactory service only as long as it is properly cared for. The lenses should be cleaned with soft lens paper. Cedar oil should not be allowed to dry on the immersion objective, but should be cleaned off with a minimal amount of xylol, care being taken not to leave any xylol on the lens lest it dissolve the cement in which the lens is mounted. The entire microscope should be protected as much as possible from dust and dirt as well as from moisture. The former is a particularly necessary precaution in city laboratories and in those where dust is prevalent; the latter, in humid climates especially near the sea coast. The bright metalled parts should be covered with a thin film of oil and the rack-and-pinion, as well as the fine adjustment, should be periodically lubricated with vaseline. When not in use, it is desirable to keep the instrument in its case or covered with [illegible]

In [illegible]

provi[illegible]

should also be kept lubricated.

Differential diagnosis often requires micro-measurements. The micro-unit is the micron, usually designated by the Greek letter "μ." This unit is 0 001 of a millimeter.

Measurements are made by placing a circular piece of glass, *the ocular micrometer*, on which accurate rulings are etched on the support within the eye-piece of the microscope. When in position this [illegible]

and the scale should be right side up. [illegible]

by the use of an object micrometer, which is a slide on which there are [illegible] graved 100 units, exactly 10 μ apart, thus making a total length of 1 mm. The object micrometer, which is the absolute gauge, is placed in the center of the microscopic field under the low-power lens, so that it is in clear focus, and so that the ocular micrometer is superimposed on it in equally clear focus. Readings are then made of the number of object-micrometer units which are exactly equal to a given number of ocular-micrometer units. Thus, if one ocular unit exactly coincides with one object unit, the value of the ocular unit is 10 μ; if 20 ocular units equal 16 object units, the value of the 20 ocular units is 16 $\times$ 10 μ or 160 μ and the value of each ocular unit is 8 μ. *Similar calibrations should be made for the high-power dry* objective and for the oil-immersion objective in combination with the same ocular, [illegible] for any other ocular to be used in

[illegible]

unit values thus secured apply only [illegible] to the particular length [illegible]

[illegible]

the same readings. Once obtained, the unit-values for the microscop[illegible] should be recorded in tabular form in a convenient place. When measurements of [illegible] to be made the values are taken in terms of ocular *units* and mi[illegible]

co[illegible]

[illegible]

This is done by the use of a *camera lucida* attached to the upper [illegible] scope tube immediately surrounding the ocular *The camera lucida* is an instrument consisting of a silvered prism, a graduated horizontal arm and a mirror, with accessory pieces for adjusting the light and centering the object. The instrument is clipped over the empty microscope tube, the ocular inserted, the mirror set at 45

degrees and the light and center adjusted. Under these conditions the image of the pencil point immediately under the mirror is reflected back into the microscope, so that the eye sees, at one and the same time, both the specimen to be sketched and the pencil point. The specimen may then be traced on a piece of white paper under the pencil point. It is convenient that the paper rest on a small drawing table which has the same elevation as the microscope stage. In order not to distort the image sketched it is necessary (1) that the mirror be set at exactly 45 degrees, and (2) that the horizontal distance from the center of the silvered prism to the mirror be the same as the vertical distance from the mirror to the drawing table Adjustments may be made by drawing out the microscope tube to the desired point The actual magnification of the tracings made may be determined by removing the specimen from under the microscope, substituting the object micrometer slide and tracing its 10 μ unit lines on the drawing paper

Theoretically the best light for the microscope is clear white skylight Direct sun's rays are disastrous to consistent microscopic examination Practically, a more uniform light is obtained from an incandescent electric light of 100-watt capacity or an equally strong mantled gas lamp, the rays being filtered through a frosted "day-light" blue glass plate, or a solution of copper sulfate in a *Florence* flask of about 250–350 ml capacity placed at focal distance between the source of light and the substage mirror of the microscope Frequently the use of the h gher powers of the binocular compound microscope requires more intense illumination than skylight admits, so that many clinical microscopists using this equipment have come to rely entirely on a uniform filtered electric lamp

Glassware Required

bottles, museum jars and aquaria, and (5) serological glassware

1. Microscopic Slides and Cover-glasses.—Two sizes of microscopic slides are required, the usual size (25 by 75 mm) and a larger size (37 by 75 mm.) The former is used for blood-films, permanent fecal films, ordinary sections and *in toto* mounts; the latter, for preliminary and concentration fecal films, and unusually large sections. The cover-glasses should consist of a supply of 22 mm squares, a smaller number of 40 by 22 mm and 50 by 22 mm sizes and occasionally a larger size to cover serial sections Both slides and cover-glasses should be of a clear, white consistency, without bubbles or streaks and should not be cloudy or etched. The slides should be of uniform medium thickness with slightly beveled, clean-cut edges, so that blood-films can be easily streaked across the slide A frosted end on

examined.

2 Staining Dishes.—These dishes are made in a variety of sizes and shapes The most satisfactory ones have ribbed partitions and accommodate from 20 to 24 ordinary slides placed back to back A staining set consists of about a dozen such jars

3 Ribbed Filter Funnels.—These funnels are for special use with the Baermann apparatus (see p 600) Eight to twelve with a flange diameter of 15 to 25 centimeters are required for a set

4. Vials, Bottles, M

homeo and shell vials,

the temporary and per

Stoll flasks and pipettes are available for the Stoll egg-counting technic. The emphasis placed on this phase of the work will determine the amount of this stock to be provided.

5. **Serological Glassware.**—For serological and immunological tests an adequate supply of Wassermann tubes, standardized pipettes and micropipettes is essential. Pyrex tubes of Wassermann size are also more useful routinely than 15 ml. centrifuge tubes for carrying out the zinc sulfate centrifugal floatation technic.

Cleaning of Glassware

nei

tio

water and dried with a clean linen towel. Used or dirty glassware is ordinarily cleaned by being immersed in the following solution:

Concentrated H_2SO_4	6 parts
$K_2Cr_2O_7$	6 parts
Water	100 parts

After soaking the articles in this solution, the laboratory assistant thoroughly rinses them in water and dries them with a non-linty cloth.

Slides and cover-glasses require special care. They may either be cleaned in the above solution or in concentrated nitric acid, rinsed thoroughly in distilled water, then passed through absolute ethyl or methyl alcohol, and dried with a fine linen towel or piece of old linen sheeting. It is frequently advisable to keep slides and cover-gl

as they

glasses,

fumes ol

should r

Other Equipment

Standard incubators are needed for culture work and a low-speed centrifuge, preferably electrically driven and having arms to carry four or eight tubes, together

streaking fecal smears

It is essential to have so

ticulate material in the stoo

prefer copper or brass scree

gauze of about 22 meshes pe

at times employed to prevent vegetable debris from rising to the surface.

Chemicals

The helminthology laboratory should be provided with the ordinary reagents and other chemicals and, in addition, an adequate stock of stains All of these are usually on the shelves of a well-equipped clinical laboratory. The salt used for concentration of helminth eggs is ordinary commercial sodium chloride, which is made up as a concentrated solution, filtered and kept in a stoppered bottle. For the zinc sulfate centrifugal floatation technic, granular zinc sulphate U. S P. is used to make up a 33 per cent solution, or more accurately a solution having a specific gravity of 1.180. (See pp 594–595.) D'Antoni's iodine stain is used for staining larvæ and is recommended for routine use for Protozoa and Helminths in feces.

There should be large stock bottles of distilled water, physiological salt solution, citrated salt solution, '
cent formalin (*e. g.*, 4
Stoll egg counts, and s
(15, 35, 50, 70, 85, 95 and 100 per cent).

For the employment of ether centrifugalization technics it is necessary to have the following reagents on hand. (1) concentrated acetic acid U. S P and hydrochloric acid U. S. P.; (2) sodium sulfate crystals in a tightly stoppered bottle, (3) the detergent Triton NE, and (4) sulfuric ether, either U S P or that employed in anesthesia.

CHAPTER XXXIII

THE COLLECTION, PREPARATION, AND PRESERVATION OF HELMINTHOLOGICAL MATERIAL

INTRODUCTION

THE most important point to be emphasized about helminthological specimens is that, wherever possible, they should be collected and studied in the living state. No small part of the inaccuracies and incompleteness in the description of

preserved material.

logical material, the clinic and the field. A laboratory which is divorced from either of these two sources of supply is greatly handicapped. The clinic provides material from human sources; the field provides material from reservoir and intermediate hosts, as well as from the human population.

Frequently it is neither possible nor desirable for the physician or the epidemiologist to fol' ay be required t of an organism, optimum resul (1) The physician or field investigator must have an intelligent understanding of the problem, obtained by special study of the subject in a laboratory where medical

source of material, he must depend on accurate clinical and biological information obtained at the time the material was collected. It would almost be better that specimens be not collected and preserved than that they be poorly treated or accompanied by inadequate notes

STUDY OF FRESH MATERIAL

This requires an future development whole. It may be th ticular type is afforded only once in a life-time or at most only infrequently Accurate, measured drawings (preferably with the camera lucida), with full notes, should be made, so as to indicate the size, shape and variation of the material, important

(see p. 577) of microfilariæ or larvæ are frequently very significant in determining the landmarks and in differentiating closely related species

In all of these preliminary observations it is essential to record whether the material was obtained from spontaneous evacuation, or without anesthesia, or at necropsy; the numb condition, whether alive, moribund or dead, and,

or organs in which they were found; likewise the pathological and clinical complications which might be directly or indirectly attributed to the parasite Care must be taken, however, not to infer causal relationships of organisms to diseased conditions which cannot be proved or which are very unlikely. If the helminth is known to be a parasite of other hosts, its percentage incidence in such hosts, as well as in man, should be noted. Moreover, any physical, biological or economic conditions which might have a bearing on the establishment or perpetuation of the infection should be recorded.

FIXATION OF MATERIAL

Fixing agents are those which terminate the life of a cell or aggregates of cells Good fixatives preserve the structure as nearly as possible like it was in the living state For satisfactory use the protoplasm is first coagulated and then hardened in such a way that it will not only be as nearly normal as possible but will resist further treatment with reagents required to prepare the material for examination

It is convenient to consider this phase of the subject under the following subtopics (1) blood-films, (2) adult worms and larvæ; (3) helminth's eggs, (4) pathological tissues, and (5) intermediate and reservoir hosts. The methods utilized in each case are at least partly dependent on the use which is to be made of the specimen,

poses

Trichinella larvæ as

given infection For

...ing of the film before staining is sufficient. For Giemsa technic, fixation in absolute methyl alcohol is a prerequisite for making thin-blood films, otherwise dehemoglobinization will occur If some time is to elapse before staining with either of these methods, fixation in

...ick-drop preparations (Fig 284) and ordinary

the film may first be air-dried, then dehemo-

with equal thickness to a size of about 1 5 cm. diameter, either in the center or on the end one-third of an absolutely clean slide, and then allowing it to become thoroughly dry, eithe

probably dirty).

hour to one hour,

film, and the slide air-dried. Washing of the film is not recommended, since it frequently removes the differential characters of the stain Special fixation in a concentrated aqueous solution of mercuric chloride is advised for permanent

...l in the living

...siological saline

rapid preserva-

, the specimens

...it CHOH), the

fixing fluid being poured into the medium containing the worms, which are meanwhile kept constantly agitated to prevent contraction The material may be left

washing in water, through

...etter histological details a

(saturated solution $HgCl_2$

in physiological medium, to which a few drops of glacial acetic acid have been added) is used. After ten to twenty-four hours the specimens are carefully but thoroughly washed, and transferred by degrees to 70 per cent alcohol, at which time alcoholic-iodine-solution should be added drop by drop to remove the remaining

(b) *Permanent Films.*—If the microfilariæ in the peripheral blood are abundant, thin films may be used; if they are scarce, thick drops should be prepared, as indicated above. Wright's or Leishman's stains are usually less satisfactory than Giemsa's. In carrying out the latter technic, dilute the stock solution 1 minim to 1 cc. of distilled water and place the slides in the dilute stain for one-half hour or more until the desired
rarely overstains.) T
cells, is stained azure,
the "sheath," if present, is tinted a delicate pink.

For more distinct staining of the "sheath" hematoxylin dyes should be used. Fulleborn recommends Bohmer's hematoxylin for this purpose. [(Solutions: (A) 1 Gm. hematoxylin crystals and 12 cc. absolute alcohol; (B) alum 1 Gm. and distilled water 240 cc. Add 2 or 3 drops of (A) to watch-glassful of (B)]. Dry dehemoglobinized smears are covered with the solution, heated until slightly steaming, rinsed off with distilled water, differentiated with acid alcohol (2 per cent HCl in 70 per cent alcohol), rinsed in dilute ammonia water (1 to 10,000), rapidly run up through the alcohols, cleared in xylol and mounted in euparal, clarite, damar or Canada balsam.

In delicate blood-film work difficulty is frequently experienced because of the variable pH of the distilled water. Under such circumstances it is desirable to substitute a buffer solution for the distilled water. The author has found the following buffer solution distinctly valuable for overcoming this difficulty with blood-films: (1) pure recrystallized acid potassium phosphate, 13.26 Gm.; (2) anhydrous dibasic sodium phosphate, 5.12 Gm.; (3) distilled water 2 liters.

For better preservation, to prevent dust accumulating on the film and for examination with oil-immersion lenses the film should be covered with a neutral medium

and other workers have successfully utilized dilute solutions of neutral red and cresyl blue in working with free-swimming trematode miracidia. A similar technic can be applied to the study of the free-swimming ciliated hexacanth embryo of pseudophyllidean cestodes.

hand, some specimens are too large or too bulky to prepare in this way. The strobila of the smaller cestodes, suc
may be mounted as a whole,
tids from typical regions for
be handled in both ways. Gordiacea and Acanthocephala are difficult to manipulate and should o
I. *In Toto*
hematoxylin
tion is relatively slight. It is a general protoplasmic stain
most satisfactory for larger objects and particularly for the genital organs of helminths, which are stained with different degrees of intensity and in different shades. Grenacher's alum-carmine and Mayer's carmalum are the carmine stains that perhaps yield most uniform results. The solutions are used without dilution and the preparations are afterwards w
overstained, weak acid may be used to
reaction if it is desired to employ the
Delafield's and most other hematox
with 10 parts of water before using, since they are very active

The length of time required for *in toto* objects varies with the size of the object and with the dilution of the ripened stain. In any event it is usually desirable to overstain and then to destain with 0 5 per cent HCl in 70 per cent alcohol, until the excess has been removed and the material is a rather light reddish mahogany It should then be thoroughly washed in distilled water and transferred to a weakly alkaline medium. The most delicate differentiation with the development of various lavender and violet hues can be obtained by using a 1 per cent lithium carbonate in distilled water Ehrlich's acid hematoxylin, which is less likely to overstain, is preferred by some stain technologists for *in toto* preparations On the whole, the author has had more success with Bullard's hematoxylin, which is prepared as follows

1 Fifty per cent alcohol, 144 cc ; glacial acetic acid, 16 cc ; hematoxylin crystals, 8 Gm.

2 Heat the above solution and add distilled water, 250 cc ; ammonium alum, 20 Gm

3 Heat to boiling and add red mercuric oxide, 8 Gm

4 Cool quickly, filter and add 95 per cent alcohol, 275 cc ; glycerin, 330 cc , glacial acetic acid, 18 cc , ammonium alum, 40 Gm

5. Keep about one week in bright sunlight to ripen and filter again before using

The specimens which have once been properly stained, differentially destained and then neutralized, should be passed rather slowly through successive grades of alcohol (35, 50, 70, 85, 95 and 100 per cent), cleared and transferred to a mounting medium The length of time required in the alcohols depends in part on the fixation, in part on the size of the specimen, and in part on the permeability of its integument No arbitrary rule can be followed on this point; the student must test out each group of specimens with respect to its special needs. In general, however, nematodes should be handled very slowly, since their integument, no matter how thin, is easily shrunken by rapid dehydration.

Clarification of dehydrated objects may be effected by the use of xylol, cedar or clove oil, or methyl salicylate. The last named is frequently the one of choice for *in toto* preparations, since it has a high refractive index, renders objects least brittle and shows least emulsion when moisture is accidentally included. On the other hand, carbol-xylol is slightly better for the rapid penetration through hardened and less permeable tissues The mounting medium should be neutral Canada balsam and damar dissolved in xylol frequently require neutralization This may be accomplished by placing a few small chips of pure marble ($CaCO_3$) in the stock bottle and letting the reaction take place over a period of months Clarite has a neutral reaction and is perhaps the most practical permanent mounting medium

II. *Sections* —For sectioning of helminth parasites, the worms may first be stained with hematoxylin before imbedding, in order that the objects may easily be seen Imbedding and sectioning technics for helminths do not differ essentially from those for other zoological or pathological specimens They require dehydration through successive grades of alcohol, clearing in xylol and gradual transfer to hard paraffin, or the transfer through ether-alcohol into celloidin Paraffin sections are entirely satisfactory for most
shelled eggs the celloidin technic is

for if sufficient material is available.
be cut 8 to 10 μ in thickness. The ribbons of paraffin coming from the cutting block, after being smoothed out by floating on warm water, are fixed to the slide in series (the slide having first been covered with a very thin film of egg-albumin fixative), dried, and the paraffin dissolved in xylol; or if the sections are celloidin, they are placed in series on the slide fixed to the slide by a thin film of collodion, and hardened.

The staining of the slides follows the hematoxylin-eosin technic. At times, however, it is desirable to counterstain larval trematodes (*e. g*, miracidia or cercaria) with ammonium-carmine after the method of Best for glycogen, in order to study the specific reaction of secretory glands. For such technic, material fixed in mercuric chloride, alcohol or formalin is suitable, since the secretory granules of these glands are not dissolved as is glycogen by a fixing agent containing water. Except in very delicate cytological work, iron-alum hematoxylin staining of sections of helminths is neither necessary nor advisable.

3. **Host Tissues Containing Helminths.**—The material is treated similarly to that employed for section
sectioned in part or in wl
grains in the intestine of
satisfactory sections. Calcareous granules and concretions may be removed by previously immersing the tissue in a weak solution (0.5 per cent) of hydrochloric acid for some days, thoroughly washing and neutralizing.

CHAPTER XXXIV

THE IDENTIFICATION AND DIFFERENTIAL DIAGNOSIS OF HELMINTH PARASITES, THEIR EGGS AND LARVÆ

INTRODUCTION

THE equipment for the diagnosis of helminths and the methods of preparation of material for study, which have been described respectively in Chapters XXXII and XXXIII of this section, are directed primarily towards one end, namely, the identification of helminth parasites and their eggs, in order that definite diagnoses may be made. Most of the information with regard to the adult worms, their eggs and the various larval stages in their life cycles has been provided in detail in Sections II to VI of this book, so that careful study of these chapters will in most cases furnish adequate data for diagnostic purposes. It seems appropriate, however, to bring together in one place information of specific diagnostic value, in order that it may be more useful to the laboratory worker. For this purpose, methods of procedure in examining human excreta and body fluids for helminth eggs and larvæ are presented.

1. EXAMINATION OF HUMAN EXCRETA AND BODY FLUIDS FOR HELMINTH EGGS AND LARVÆ

(For necessary equipment see Chapter XXXII.)

Diagnostic Procedures for the Recovery of Helminths, their Eggs and Larvæ, in Human Excreta.—For convenience this topic is divided into three subtopics, each dealing with one of the three common types of human excreta, the urine, sputum and feces

Urine.—In heavy infections either *Schistosoma hæmatobium* or *Dioctophyma* eggs can be readily recovered from the muco-purulent settlings after the urine has been allowed to stand for a few moments in a urinalysis glass. A small portion of the sediment is taken up in a capillary pipette, placed on a fecal slide and examined under a cover-glass with low power of the microscope. If the infection is light, a representative specimen should be centrifugalized at 1500 revolutions per minute and some of the sediment examined. Microfilariæ of *Wuchereria bancrofti* in chylous urine, or larvæ or adult rhabditoid nematodes which are accidental residents of the urino-genital tract, as well as Protozoa, if present, may be recovered from the urine by similar methods of concentration. Helminths or eggs passed in urine may be permanently preserved by the methods described in Chapter XXXIII.

Sputum.—In patients suspected of having helminthic infections of the respiratory passages, the mouth is first thoroughly rinsed with hydrogen peroxide solution and the sputum then passed into a sputum-jar. A small portion is transferred to a slide by use of a tooth-pick or specimen applicator mounted with a cover-glass or [illegible]

de ... (due either to ... amount of S. japonicum) is suspected ... e ... r ... under Topic ... chapter should be employed. (p. 590)

It should be remembered that fecal smears must be thin enough to view clearly all of the objects under the cover-glass. Only experience will provide facility in determining which types of specimens must be streaked thin and which ones may be streaked somewhat thicker.

(a) *Evacuated Mature Worms or Portions of Worms.*—Entire helminths (*Ascaris*, ... *robius*, etc.) are at times evacuated in feces and may ... ar anatomical characters. In patients infected with ... *T. solium*, gravid proglottids are almost invariably passed in feces or crawl out the anus. They not only occur at times when the feces are negative for eggs but also constitute the sole method of specific differentiation of these two *Tænias* before therapeusis has been instituted. The unpreserved, moist proglottids are flattened between two broad slides (37 by 75 mm.) and are examined with a hand lens to determine the number of main lateral uterine arms on each side of the primary uterine stem (*Vide* Fig. 132 1, 2)

(b) ...

—Alt ... ing the anal region for detecting *Enterobius vermicularis* infections, Heller (1876) apparently first recommended the use of an anal scraper or swab to obtain material for microscopical examination for *Enterobius* eggs. Since Heller's day spatulas, curettes, glass tubes and rods, metal ... obtain feces and mucus from ... devised a much more convenie... yields The applicator, known as the NIH cellophane anal swab, consists of a glass rod tipped with cellophane held in place with a rubber band, and is employed to swab the perianal area of the patient. The cellophane with adhering material is removed from the rod, is flattened between two glass slides and examined for eggs

...

the deposit examined under a microscope. The pestle is easily cleaned in water

...

preferred technic in obtaining eggs of *Tænia solium*.

(c) *Diagnostic Procedures for the Recovery of Helminth Embryos or Larvæ from Blood and Lymph.*—Thick blood-films may be prepared by the technic de-

scribed in Chapter XXXIII, or fresh blood may be defibrinated by vigorous shaking, then dehemoglobinized and centrifugalized Nematode larvæ, if present, will be found in the bottom layer and can be drawn off with a pipette *Trichinella* larvæ and *microfilariæ*, even when present in small numbers, may be recovered from these fluids by this technic

2 IDENTIFICATION OF ADULT WORMS AND LARVÆ IN ADVANCED STAGES OF DEVELOPMENT

Adult helminths are most commonly found in the intestinal tract, although a considerable number of species are found in other localities, such as the biliary passages, lungs, portal circulation, lymphatics and subcutaneous tissues Occasionally these worms are expelled spontaneously, but the larger number is recovered after
necropsy In the majority of
eggs of the parasite passed in

For the diagnosis of adult helminths the detailed descriptions provided for each species in Section II to VI of this book should be consulted

3. IDENTIFICATION OF EGGS AND LARVÆ DEVELOPING IN EGG MEMBRANES, DERIVED FROM ADULT WORMS IN HUMAN INFECTIONS

The majority of helminth eggs are evacuated in the patient's feces A few are recovered from urine and sputum "Ensheathed" microfilariæ (*e. g*, enveloped in an elongated egg membrane provided by the parent worm) are found in blood, lymph and serous exudates Eggs of a few species are hatched in the uterus of the parent worm A few are hatched at the time of egg-laying The largest number, however, is oviposited in the unhatched condition Some of these contain fully embryonated larvæ which are capable of hatching as soon as the egg comes into a favorable environment. Others require a period of several days to several weeks before the enclosed embryos become mature and are ready to escape from eggshell

The accompanying figures (Fig. 285 *A-Z*) will serve as an aid in the identification of all but the rarer (*i e*, incidental) species of helminth eggs recovered from the feces, urine or sputum.

4 DIAGNOSTIC KEY FOR THE IDENTIFICATION OF THE MORE COMMON HELMINTH EGGS AND LARVÆ

1 (19, 24) Eggs 2
2 (14). *Provided with an operculum* 3
3 (9). *Unembryonated* 4
4 (5). *In sputum.* Broadly ovoidal, dark golden-brown, moderately thick-shelled, with relatively flat but distinct operculum and thickened abopercular end; size: 80–118 × 48 — 60 μ
Paragonimus westermani (Fig 285, V).
5 (4) *In feces* 6
6 (7, 8). Large, hen's-egg-shaped, light yellowish or greenish-brown, with relatively thin shell and small, indistinct operculum
i. Size: 130–150 × 63–90 μ
Fasciola hepatica and *Fasciolopsis buski* (Fig 285, *P*)
ii Size: 83–116 × 58–69 μ
Echinostoma ilocanum (Fig 83.1, p 191).
iii. Size: 120–130 × 80–90 μ
Echinostoma malayanum (p 192).

7 (6, 8). Long, narrowly ovoidal to elliptical, with a small, distinctly domed operculum; size: 150–170 × 60–70 μ. . . . . . *Gastrodiscoides hominis* (Fig. 285, W).

8 (6, 7). *i.* Broadly barrel-shaped, relatively thick-shelled, with a broad, slightly domed operculum; size: ca. 70 × 45 μ *Diphyllobothrium latum* (Fig. 285, M).

ii. Narrowly barrel-shaped, relatively thick-shelled, with a narrow, distinctly domed operculum; size: ca. 60 × 35 μ *Diphyllobothrium houghtoni, D. mansoni, D. erinacei, D. decipiens*, etc. (Fig. 285, N).

Likewise *Paragonimus westermani* eggs in sputum may swallowed and passed in the feces. See "4" above.

9 (3). *Fully embryonated* 10

10 (11). Medium-sized (38–45 × 22–30 μ), with a thick, dark-brown shell, having a distinctly domed operculum . . . . . . *Dicrocœlium dendriticum* (Fig. 285, Q).

LEGEND FOR FIG. 285.

FIG. 285.—Diagnostic chart of the characteristic eggs and larvæ of the more common helminths parasitizing man. **A** *Ascaris lumbricoides*, unsegmented fertile egg, usually with bile-stained outer shell, passed in feces, **B** *A. lumbricoides*, infertile egg, usually with bile-stained outer shell, passed in feces, **C** *Enterobius vermicularis* (*Oxyuris vermicularis*, pinworm or seatworm), with completely developed larva, passed in feces or more usually deposited by

worm"), with completely developed first-stage (rhabditoid) larva, passed in constipated stool or developed in feces that have stood twenty-four to forty-eight hours in the laboratory; **F** *A. duodenale* ("Old World hookworm") or *N. americanus* ("American hookworm"), anterior extremity of hatched rhabditoid larva, showing long, narrow, buccal cavity (contrast with anterior end of **G**), **G** *Strongyloides stercoralis*, rhabditoid larva passed in feces, showing very short buccal cavity (contrast with **F**), **H** *Trichostrongylus*, characteristic morula-stage egg passed in feces, **I** *Trichocephalus trichiurus* (*Trichuris trichiura* or whipworm), with unsegmented embryo, usually with bile-stained outer shell, passed in feces; **J** *Tænia saginata* (beef tapeworm) or *T. solium* (pork tapeworm), with fully embryonated oncosphere, with dark brown outer shell, passed in feces; **K** *Hymenolepis nana* (dwarf tapeworm), with fully embryonated oncosphere, passed in feces, **L** *Hymenolepis diminuta* (rat tapeworm), with fully

containing several fully embryonated oncospheres, as passed in feces or expressed from disintegrating gravid proglottid, **P** *Fasciolopsis buski* (large intestinal fluke) or *Fasciola hepatica* (sheep liver fluke), unembryonated, as pas
and/or biliary drainage, **Q** *Dicrocœlium dendriticum*,
feces or obtained by duodenal or biliary drainage; **R** [illegible] developed miracidium, passed miracidium, passed in feces, **S** *Metagonimus yokogawai*, with developed miracidium, passed in feces or obtained by in feces, **T** *Opisthorchis felineus*, with developed miracidium, passed in feces or obtained by duodenal or biliary drainage; **U** *Clonorchis sinensis* (Chinese liver fluke), with developed miracidium, passed in feces or obtained by duodenal or biliary drainage, **V** *Paragonimus*

feces, **Z** *Schistosoma japonicum* (Oriental blood fluke), with developed miracidium, passed in feces

R, S, T, and *U*, × 666, all other figures, × 333. (Original.)

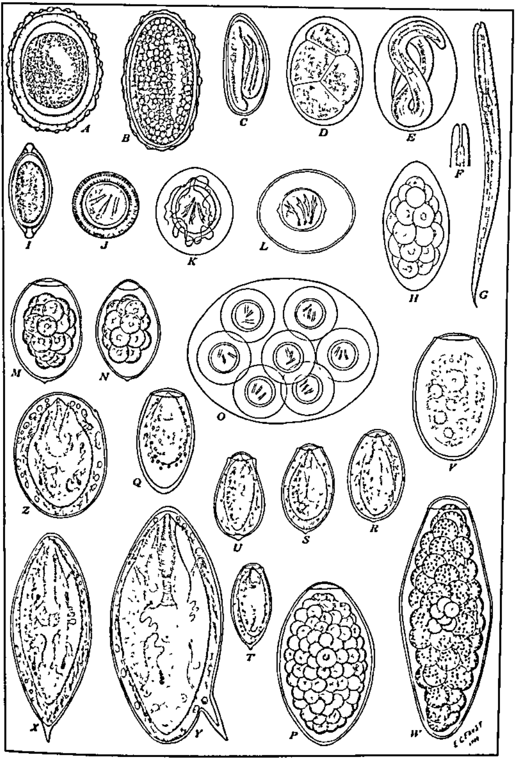

FIG. 285

11 (10). Minute eggs,

12 (13). With enclosed 12
lytic glands. arranged
i. Size: ca. 30 × 11 μ . . . . .
Opisthorchis felineus (Fig. 285 *T*).
ii. Size: 27.3–35.1 × 11.7–19.5 μ. . . . . . .
Clonorchis sinensis (Fig. 285, *U*).

13 (12). With enclosed miracidium having bilateral symmetry of lytic glands.
i. Size: 28–30 × 15–17 μ. . . . . . .
Heterophyes heterophyes (Fig. 285, *R*).
ii. Size: 26.5–28 × 15.5–17 μ. . . . .
Metagonimus yokogawai (Fig. 285, *S*).

14 (2). *Lacking an operculum* 15

15 (16, 17, 18). *Fully embryonated, containing a rhabditoid larva;* egg medium-sized (50–60 × 20–30 μ); narrowly ovoidal, relatively thick-shelled, flattened on one side
Enterobius vermicularis (Fig. 285, *C*).

16 (15, 17, 18). *Fully embryonated, containing a ciliated larva;* with a light yellowish-brown shell having a spine
i.

ii. spine; size: 114–175 × 45–68 μ
Schistosoma mansoni (Fig. 285, *Y*).
iii. Broadly ovoidal, with an inconspicuous, small, hooked spine; size: 70–100 × 50–65 μ
Schistosoma japonicum (Fig. 285, *Z*).

17 (15, 16, 18). *Fully embryonated, containing a non-ciliated embryo (oncosphere)* possessing 3 pairs of hooklets.
i. With a thick, brown, radially-channelled, outer shell; subspherical; size: 31 to 43 μ in diameter . . . .
Tænia saginata and *Tænia solium* (Fig. 285, *J*).
ii. With a thin, hyaline, outer shell; polar thickenings with filaments on inner shell; spherical to subspherical; size: 30–47 μ in diameter *Hymenolepis nana* (Fig. 285, *K*).
iii. With a moderately thin, light yellowish-brown, outer shell; polar thickenings without filaments on inner shell; subspherical; size: 60–79 × 72–86 μ

iv. Wi . . . enclosed in a mother embryonic membrane
Dipylidium caninum (Fig. 285, *O*).

18 (15, 16, 17). *Unembryonated or incompletely embryonated.*

i. Shell narrowly barrel-shaped, dark brown, with a plug-like, semi-opaque, whitish swelling at each end, size: 50–54 × 22–23 μ
Trichocephalus trichiurus (synonym: *Trichuris trichiura*) (Fig. 285, *I*)

ii. Shell usually provided with an outer, mammillated, albuminoid cover, characteristically bile-stained, with thick, hyaline, outer shell, fertile eggs broadly ovoidal, size: 45–75 × 35–50 μ; infertile eggs irregularly elongated-ovoidal; size 88–93.5 × 38.5 — 44 μ
Ascaris lumbricoides (Fig. 285, *A*, *B*)

iii. Shell thin, hyaline, elongated-ovoidal, with narrowly rounded ends; typically with morula-stage embryo, size. 73–80 × 40–46 μ *Trichostrongylus colubriformis* or *T. probolurus*, 84–90 × 46–50 μ
T. vitrinus; 75–91 × 39–47 μ
T. orientalis (Fig. 285, *H*).

iv. Shell thin, hyaline, ovoidal, with bluntly rounded ends, size: ca. 60 × 40 μ *Ancylostoma duodenale* or *A. braziliense*, 64–76 × 36–40 μ *Necator americanus* (Fig. 285, *D*, *E*); 50–58 × 30–34 μ parasitic generation of *Strongyloides stercoralis* (rarely found unhatched in feces).

19 (1, 24). LARVÆ 20

20 (21, 22, 23) Moderately short, with muscular esophagus.

i.

(Fig 285, *G*)

ii. Esophagus having only a posterior bulbar swelling; pre-esophageal chamber long and narrow
Ancylostoma or *Necator* (rhabditoid larva) (Fig 285, *F*)

iii. Esophagus having both a median and a posterior bulbar swelling
Most species of *Rhabditis* (Fig 205 *D*, p 389).

21 (20, 22, 23). With long, attenuate, caudal extension and with muscular esophagus

i. Esophagus having both a median and a posterior bulbar distention
Some species of *Rhabditis*

ii. Esophagus having only a slight posterior bulbar swelling; with distinctly striated cuticula and a pair of minute pockets on either side of

the anus; size: 500–750 × 15–25 μ. . . . . . *Dracunculus medinensis* (discharged by mother worm from cutaneous lesion into water). (Fig. 280 *D*).

22 (20, 21, 23). Elongate, narrow, with long, narrow, muscular esophagus.

i. With minute forking at caudal extremity. . . . *Strongyloides stercoralis* (filariform larva). (Fig. 207 *B*).

ii. With sharply pointed caudal extremity. . . . *Ancylostoma* or *Necator* (filariform larva). (Fig. 222).

23 (20, 21, 22). Elongate, narrow, characteristically coiled, with non-muscular esophagus . . . . *Trichinella spiralis* (rarely recovered in feces or blood). (Fig. 195*C*).

24 (1, 19). Microfilariæ 25

25 (26). *Provided with a sheath.*

i. Without nuclei in tip of tail; in circulating blood, in most endemic areas exhibiting strict nocturnal periodicity; size: 244–296 × 8 μ . . *Microfilaria bancrofti* (Fig. 260).

ii. With two distinct nuclei at tip of tail; in circulating blood, exhibiting partial nocturnal periodicity; size: 177–230 × 3.4–3.8 μ . . . *Microfilaria malayi* (Fig. 270).

iii. With nuclei extending into tip of tail; in circulating blood, exhibiting partial diurnal periodicity; size: 250–300 × 6–8.5 μ *Microfilaria loa* (Fig 278).

26 (25). *Without a sheath.*

i. With nuclei extending into tip of tail; in circulating blood, exhibiting slight nocturnal periodicity; size: [illegible]

ii. [illegible] periodic; size: 205–208 × 5 μ *Microfilaria ozzardi* (Fig. 276 *B*).

iii. Without nuclei in tip of tail; migrating in skin and subcutaneous tissues, rarely in blood, size: 285–368 × 6–9 μ and 150–287 × 5–7 μ *Microfilaria volvulus* (Fig. 271*C*).

5. FECAL CONTAMINATORS, ARTEFACTS, AND PROTOZOAN CYSTS LIABLE TO BE CONFUSED WITH PARASITIC HELMINTHS AND THEIR EGGS

[illegible]

of these are contaminators or artefacts. A considerable [illegible]

others are animal cells; still others are artefacts pure and simple. Mucus casts formed in the respiratory, urinary and intestinal tracts may more or less resemble adult helminths, but inspection, even with a good hand lens, will prove that they are not genuine organisms. The long fibers of many semi-woody plants and such fruits as the banana, when digested out of their tissue-matrix, may also be at first mistaken for nematodes, but examination with low power of the microscope will serve to dispel this first impression.

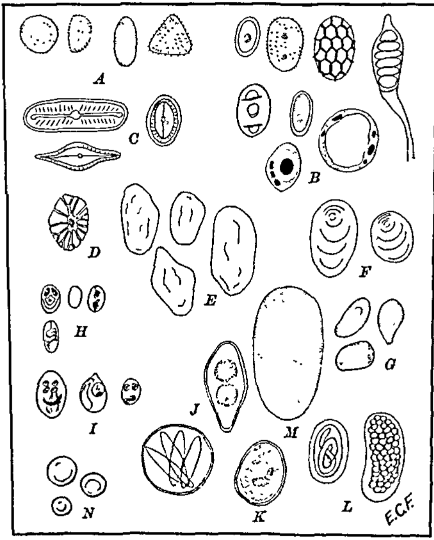

FIG. 280.—Fecal contaminators, artefacts and protozoan cysts in human feces liable to be confused with parasitic helminth eggs. *A*, pollen grains, *B*, fungus and yeast spores, *C*, diatoms, *D*, stone cell of fruits such as the pear, *E*, parenchymatous cells of vegetables such as the Cucurbitaceæ, *F*, starch grains, *G*, partly digested protein particles, *H*, myxosporidian and microsporidian cysts ingested in parasitized animal tissue, *I*, cysts of intestinal protozoa, *J*, coccidia cysts, *K*, *Balantidium* cyst, *L*, eggs of nematodes accidentally ingested, *M*, egg of mite, *N*, oil globules. × 500-800. (Partly original, partly compiled from various sources.)

tiate them. The majority of such cells are referable to pollen grains (Fig. 286A) fungus or yeast spores (Fig. 286B), diatoms (Fig. 286C), stone cells of such plants as pears (Fig. 286D), or parenchymatous cells of succulent plants such as melons (Fig. 286E). Pollen grains may be spherical, ovoidal, tetrahedral or elongate, and may be covered with a smooth or sculptured epidermis. They are of a constant size for each species. Internally they are readily distinguished from helminth eggs. Fungus spores and yeast cells are usually smaller than helminth eggs; they may be ovoidal or subspherical and in some cases may have a stipe-attachment at one end. They are constant in size, but are usually easy to differentiate from helminth eggs.

[illegible]

are irregularly ovoidal, polygonal or elongate, inconstant in size, and slightly wrinkled superficially. Internally they are usually devoid of structure, although a nucleus may at times be found. Furthermore, starch grains, intact or partially digested (Fig 286F), may at times be confused with helminth eggs, but may be readily differentiated, since they are solid structures consisting of laminæ laid down around an acentric core. Likewise particles of protein (Fig. 286G), the contours of

[illegible]

sites. The only members of the former group (Fig. 286 H and J, lower left) thus far observed are microsporidi [illegible] ingested in parasitized fish flesh. The cys [illegible] in shape, much smaller than [illegible] which serve to differentiate t[illegible] spherical (20 to 45 μ in diameter) and contain four characteristic internal spore-forming bodies. The cyst of the coccidian parasite in the human intestine (Isospora hominis) is irreg[illegible] by 12.5 to 16 μ, [illegible] Balantidium coli, [illegible] cal, measure about 50 to 60 μ, and contain the encysted protozoan, which [illegible] reniform macronucleus and a distinct cytostome. In addition to the eggs of the plant nematode, *Heterodera marioni*, which have been observed in human feces by several investigators, the present author has found in human feces the eggs of *Physaloptera, Capillaria hepatica, Dicrocœlium dendriticum*, and *Fasciola hepatica*, which were not derived from human infections but from ingested animal tissues infected with the parent worms.

Again, eggs of mites (Fig 286M) whic[illegible] confused with eggs of helminths. Such eggs, [illegible] and either contain a homo- ends, are [illegible] genous sen[illegible]

Finally, [illegible] to be eliminated from consideration as objects which might be [illegible] helminth eggs.

6. METHODS FOR THE QUALITATIVE AND QUANTITATIVE DIAGNOSIS OF HELMINTH EGGS AND LARVÆ

The *direct fecal film* should always be made and examined in the diagnosis of suspected protozoan and helminthic infections of the intestinal tract as well as in infections of other organs and tissues from which the parasite

objects escape into the lumen of the bowel and are evacuated in the feces. In heavy infections this technic will serve to discover the parasite. Moreover, flecks of blood and mucus in the stool should be examined, since they yield at times a nest of diagnosable objects. If quantitative studies are contemplated the Stoll technic (*vide infra*) and the Beaver technic (*vide infra*) may be employed.

Concentration technics are designed to remove a considerable amount of the fecal detritus without a comparable amount of parasite objects, so that the residuum contains several times as many parasites per unit volume of material as were present in the unprocessed stool. The efficiency of a particular concentration technic depends on (a) the ratio of loss of non-parasite material to parasites, (b) the simplicity of the operation, (c) the time consumed and (d) the diagnosability of the parasite objects obtained in the concentrate.

A. Eggs in Feces.—The concentration of helminth eggs by various methods has a two-fold purpose, (1) the detection of eggs in light infections where ordinary fecal smears are negative, and (2) the saving of time in diagnosis due to the yield of a larger number of eggs per microscopic field. In addition, the more refined technics

age and undigested food; (4) centrifugalization; (5) floatation, (6) centrifugal floatation, and (7) ether concentration technics. These will be taken up *ad seriatim* and their several merits and shortcomings considered.

cephalus, *Tænia* and *Hymenolepis* eggs the method gives excellent results. *Clonor-*

2 **Sedimentation.**—Ten to 100 Gm. of the fecal specimen are thoroughly comminuted in ten to twenty times their volume of tap water and then allowed to settle out After an hour or two the top two-thirds with the floating débris is either carefully poured off or siphoned off, water is added to near the top of the container and the fecal material thoroughly mixed with it. This procedure is repeated several times, until the supernatant fluid is relatively clear. After a final removal of water

helminth eggs passed in feces, as it produces no distortion of the eggs. It is especially recommended for recovery of the eggs of *Schistosoma japonicum* (Faust and Meleney, 1924; Andrews, 1935) and *S. mansoni* (Faust and Hoffman, 1934) The only serious drawback to its routine use is the time consumed. Furthermore, it is not dependable for quantitative studies.

Faust, Ingalls and See (1946) confirmed for *Schistosoma japonicum* the earlier observations of Faust and Hoffman (l c), that 0 5 per cent glycerine added to tap

water causes increased "wetting" and more rapid sedimentation, minimizes the number of eggs decanted and provides a yield up to about 25-fold that of the unprocessed stool. It is desirable to strain out the larger detritus in the stool through surgical gauze having about 22 meshes to the linear inch, using four thicknesses which have been previously soaked in water and the excess of water squeezed out. The gauze is then stretched loosely over a funnel of appropriate size and the emulsified feces poured through into the sedimentation glass. Very few eggs are trapped in the gauze unless there is a considerable amount of mucus in the stool. After one hour the first decantation is made, forty-five minutes later a second, and thirty minutes later a third and last one. Measured amounts of the sediment in the bottom are then removed to a microscopic slide and mounted with a 40 x 22 mm coverglass. Eggs of all types in the stool without loss of viability due to the technic are present in unusually high concentrates in the sediment. It is probably the most practical method for obtaining immature, fully mature and degenerate eggs of *Schistosoma japonicum* and *S. mansoni* for diagnosis in the same proportion in which they occur in the stool.

Jahnes and Hodges (1947) claim that 10 per cent ethyl alcohol in water (sp. gr. 0.986), is two-fold superior to 0.5 per cent glycerinated water for recovery of *Schistosoma* eggs, that the eggs obtained are not damaged and later hatch.

3. **Straining Out Coarse Roughage and Undigested Food.**—This is effected by using a bolting cloth of 5 meshes to the millimeter or bronze wire screen of 30 to 120 meshes per linear inch. It eliminates the bulky particles and in so doing concentrates the egg-containing fecal elements. Cobb (1904) used this technic for the recovery of *Fasciola hepatica* eggs in sheep feces. The process is relatively slow and requires considerable care in cleaning in order to wash out eggs that might become lodged in the meshes of the finer sieves.

A metal basket with a fine-meshed wire sieve is very useful in searching for small

meshes to the linear inch,
in centrifuge tubes and s
tant liquid is poured off,
repeated two or more times until the supernatant fluid is clear. The eggs and larvæ, which are all heavier than the ordinary fecal elements, are thrown to the bottom of the tube, so that the examiner is permitted to obtain moderate concentration in the sediment. It is quite efficient for hookworm and *Ascaris* eggs, and very helpful in the recovery of small numbers of operculate eggs, *Trichocephalus* eggs and *Strongyloides* larvæ. This technic was used by Pepper (1908) and was extensively utilized by Howard (1915, 1919) in hookworm surveys in British Guiana. Lane states (1928) that its effective concentration is much less than was
or

a
sedimentation but more rapid. The steps are ... Erlenmeyer flask containing about 100 cc. tepid tap water; (2) the suspension is strained through two
are shaken up thoroughly for one to two minutes in a 125 cc. Erlenmeyer flask con-
taining about 100 cc. tepid tap water; (2) the suspension is strained through two
layers of wet g ... with a teated bottom; (3) this is
spun in the ce
poured off, 40° C
(4) until supern ... *Schistosoma* eggs, add
22 x 40 mm coverglass; (7) if not positive for *Schistosoma* eggs, add
water to the sediment and allow to stand until morning, then look for hatched miracidia.

5. **Floatation.**—Introduced by Bass, in 1906, the value of this technic depends on the fact that saturated salt solutions have a greater specific gravity than most helminth eggs, so that eggs in feces which have been mixed with these solutions

eggs, as *Fasciolopsis*, *Echinochasmus* and *Diphyllobothrium* "pop" open or shrink in brine or other concentrated solutions and sink to the bottom. The smaller, thick-shelled eggs, such as those of *Clonorchis*, *Metagonimus* and *Dicrocœlium*, are denser than the saline medium and sink rather than float. *Schistosoma* eggs shrink into an unrecognizable condition in a brine solution.

The brine solution may be made up to saturation by using crude salt, which usually has a slightly greater density than refined salt. The solution should be filtered and kept in a stoppered bottle The specific gravity will vary between 1 120 and 1 210, depending in part on the temperature and in part on the crude elements in the brine but for efficient use should read about 1.200.

Kofoid-Barber Brine Floatation-loop Technic (1918)—This consists essentially of the comminuting of the fecal specimens in paraffined cups in which they have been collected, with two to three times their volume of brine, forcing the coarse roughage

drawback to the technic, since the number of eggs in the surface film removed varies

fecal specimen with 10 to 20 parts of brine in a cylinder-container of about 2 5 cm. diameter, the liquid being sufficient so that the mixture comes exactly to the surface of the container and forms a definite meniscus. A grease-free fecal slide (37 x 75 mm) is carefully superimposed upon the meniscus and allowed to remain for one hour, after which it is carefully removed, inverted and direct examination made of the film attached to the slide In the author's experience the optimum time is much shorter, ranging from ten to fifteen minutes If the procedure is properly carried out, a large proportion of all the eggs in the specimen should have floated to the surface film and have been removed. This method is one giving maximum results for the least effort in field operation where non-operculate eggs exclusive of *Schistosoma* are to be diagnosed. It effects a greater concentration of eggs than the Kofoid-Barber technic, although it cannot be used as an accurate egg-count technic.

Zinc Sulfate Floatation —As a simplification of the zinc sulfate centrifugal floatation technic developed by Faust *et al* (1938, 1939, *vide infra*), Otto, Hewitt and Strahan (1941) developed a direct floatation technic employing zinc sulfate with specific gravity 1 180, without screening the fecal material. The operation is performed in shell vials (5 x 1.8 cm), which contain the fecal sample thoroughly suspended in the solution which fills the vial to the brim. Well-cleaned 22 mm. square cover glasses are superimposed on the surface film to remove the concentrate of helminth's eggs and protozoan cysts. It is claimed that the yield of eggs is appreciably greater than with the original technic, although that of protozoan cysts is less.

6 **Centrifugal Floatation.**—(*a*) *Lane's Direct Centrifugal Floatation or D. C. F.* (1922) —This technic was developed by Lane in an attempt to overcome some of the difficulties inherent in the simpler methods. Without question it is one of the most precise and delicate methods thus far devised and concentrates in the surface film all but a negligible amount of the eggs of *Ascaris*, hookworm, *Trichocephalus* and *Trichostrongylus* from a specimen. It is an elaboration and refinement of the Bass method of 1909, in which feces were first strained through a sieve, then successively centrifuged in water, heavy salt solutions, and water again.

One cubic centimeter of feces is measured out from the specimen and placed in a special ground-top centrifuge tube, which is filled with tap water to within 25 mm of the top. The tube is then corked,
thoroughly commingled with the water. :
and spun for one minute at 1000 revolu
next poured off and the tube is nearly filled with a saturated brine solution, corked and agitated until the suspension is homogenous. The tube is then returned to the carriage, filled brim-full with additional brine solution, and covered with a thick cover-glass which is anchored to the four horns of the special carriage bucket. It is then centrifugalized for one minute at 1000 revolutions per minute and the cover-glass removed, placed on a plasticine support on a slide and examined as a hanging drop. With a brine solution of 1200 specific gravity a rapid-lift direct centrifugal floatation will deliver 70 to 95 per cent of all of the eggs in the sample on the first spin, while second and third spins will deliver an appreciable balance and a fourth spin a relatively negligible number, if any. This technic is, therefore, sufficiently accurate for estimating the number of *Ascaris*, hookworm or *Trichocephalus* worms present in any given infection, using the number of eggs per female worm per gram of feces as the conversion figure. The method is, however, too complicated for field work, although it is suitable for a central diagnostic laboratory, where maximum accuracy is desired and good technical assistance is available.

(b) *The Hamburg Cover-glass Technic* (1926, 1927).—This technic, as devised by Fulleborn and his associates, makes use of saline floatation for enriching the yield of eggs, and provides a quantitative accuracy without the time-consuming labors of the Lane method. A glass or metal cylinder of about 5 cm. diameter and 3.5 cm height is provided with a depression in the bottom which will hold 1 Gm. of formed feces. The container is then nearly filled with concentrated salt solution and the feces thoroughly comminuted. Three 18 mm. square cover-glasses are carefully placed on the surface and allowed to remain for 10 minutes. These are then removed with a cover-glass forceps and placed on microscopic slides, film-side-down. All of the eggs under each cover-glass are counted and the average of the three counts taken. To compute the total number of eggs in the
multiplied by 7.0, if the eggs number 20–40; by
they number 70–90, and by 9.5, if they number

centrifugal floatation technic are as follows: (1) A fecal suspension is prepared by thoroughly mixing about 10 parts of lukewarm tap-water with one part of the stool
specimen
pension
Wassern
galized for 45 to 60 seconds at a speed of about 2300 rpm, or top speed, using an International clinical centrifuge. The supernatant fluid is poured off, 2 or 3 cc. of water are added, the sediment is broken up b
water is added to fill the tube (4) Procedure
until the supernatant fluid is clear. (5) The
3 to 4 cc. of zinc sulfate solution of the specific gravity 1.180 (33 per cent solution) are added, the packed sediment is broken up, and enough zinc sulfate solution is
add fill the tube to about one half inch of the rim (6) The tube is centri-
fug

fecal slide, one drop of D'Antoni's iodine stain is added, and the preparation agitated manually to insure uniform staining. (8) The preparation is mounted with a 22 mm.

technic for centrifugal flotation ... 1.180 sp. gr., the quantitative accuracy of the Lane technic is achieved for both the eggs of helminths and protozoan cysts Hood (1947) employed the zinc sulfate technic as a quantitative check on the Stoll dilution counts (*vide infra* "Stoll Egg-count Technic"), using 500 hookworm-positive stool specimens. She found that in light infections (*i. e.*, one to 40 eggs per slide by the zinc sulfate technic) 61.2 per *cent were missed by the Stoll method. Since the zinc sulfate concentrate provided* an average count 12-fold that of the Stoll count, a conversion formula, *viz*,

$$\frac{ZnSO_4 \text{ count} \times 200}{12} = \text{eggs per cc. of stool.}$$

Watson (1947) has modified the original zinc sulfate technic (1) by omitting the screening process and (2) by using a superimposed round cover-glass with a thin film of Mayer's albumin fixative on its lower side, applied to a ground-glass top of the Wassermann tube, which is spun in the centrifuge at 1500 rpm for 3 minutes.

Summers (1942) developed a modification of the zinc sulfate technic for use with formalinized feces. The solution is made up to specific gravity 1.200, is mixed with the feces and the emulsion is processed without straining. While a satisfactory yield of diagnosable eggs is obtained, protozoan cysts are shrunken and their diagnostic characteristics impared.

The zinc sulfate technic, like the brine technics, is not suitable for concentration of *Schistosoma* eggs, those of *Clonorchis*, *Opisthorchis*, or operculate types such as *Fasciola*, *Fasciolopsis*, *Paragonimus* and *Diphyllobothrium*.

provides a
unstained,

7. Acid-...

tion of the fecal detritus, mucus and fatty material and the sedimentation of the heavy particles including cysts and eggs Several acids have been utilized, including hydrochloric acid (Teleman, 1908), citric acid (Carles and Barthelemy (1917), acetic acid (De Rivas, 1928), and modifications of the HCl technic.

a Telemann Technic (1908).—A small amount of feces is emulsified with *concentrated HCl and ether, equal parts, the suspension strained through a hair sieve,* centrifugalized for one minute and the sediment examined.

b Carles-Barthelemy Technic (1917)—The feces are emulsified in 10 per cent

De Rivas Method (1928).—(1) About 1 *to 2 Gm. of feces are placed in approximately* 10 cc. of a 5 per cent solution of acetic acid in a 15 cc. centrifuge tube and thoroughly comminuted by shaking; (2) after allowing the suspension to stand for about 30 seconds, to permit the heavy particles to settle to the bottom of the tube,

the supernatant suspension is passed through one or two layers of cheesecloth into another centrifuge tube until the latter tube is nearly half full; (3) an equal amount of ether is added, a rubber stopper is placed in the mouth of the tube and the tube thoroughly shaken for about 30 seconds; (4) the tube with its contents is then centrifugalized for 2 to 5 minutes. (The tube now contains four layers: (a) an ether top layer, (b) a detritus interphase layer, (c) the acid layer and (d) a small amount of sediment at the bottom, (5) all but the sediment is poured off and the latter is removed with a capillary pipette to a microscopic slide for examination.

c. Mathieson and Stoll Technic (1945).—One Gm. of feces is suspended in 5 cc. of a 15 per cent solution of HCl (40 cc. HCl conc. made up to 100 cc., with specific

immature and degenerate ones.

d Weller-Dammin Technic (1946).—This consists of the addition of 0.06 cc. of a concentrated solution of the detergent Triton NE to the 15 per cent solution of HCl of the Mathieson-Stoll technic It provides a considerably higher yield of diagnosable *Schistosoma* eggs when carried out in parallel with the Mathieson-Stoll technic.

e Faust-Ingalls-See Technic (1946).—This is similar to the Weller-Dammin technic except that the feces are emulsified in a combination of HCl, Na_2SO_4 and Triton NE; or Na_2SO_4 completely replaces HCl. The first formula is, 2 5 cc. HCl + 2.5 cc Na_2SO_4 (sp gr. 1 080) + 0.06 cc. Triton NE; the second formula, 5 cc. Na_2SO_4 (sp. gr 1 080) + 0 06 cc Triton NE. Both of these methods provide a high yield of superior quality *Schistosoma* eggs. They are likewise well adapted to concentrate very small numbers of *Clonorchis* eggs.

f Loughlin Stoll Acid-Ether-Xylol (AEX) Technic.—(1) Measure 4 ml. (or 4 Gm) feces into a Stoll counting flask containing 56 ml water; (2) add several glass beads, shake and set aside over-night in refrigerator; next morning shake vigorously to secure complete comminution, (3) after securing thorough distribution of the eggs by shaking, transfer 1 5 ml. suspension to a 15 ml. pointed centrifuge tube; (4) add ... HCl (20 ml conc. HCl in 100 ml water), close with rubber

sediment to slide, mount with cover glass and examine The procedure is ... to be superior to the Telemann and Lane technics for infertile *Ascaris*, *Trichocephalus*

eggs may fail to
contain a few egg
of the stool should be carried out in 0 5 per cent glycerinated water ...
Although ether technics are time-saving, they are not cheap for survey work and should be reserved for special cases.

... d for the accurate
Strictly speaking,
... iginal method three
... aduated up to 45 cc.
grams of feces are weighted into a large, thick-glass ... 45 cc mark. Ten small
Decinormal sodium hydroxide solut
glass beads are then added, the tu
until the mixture is homogenized

20 per cent. Multiplying the total count per gram of feces by the average daily output of feces per individual gives the total egg production *per diem*.

The technic has been modified and simplified as follows (Stoll and Hausheer, 1926) Into a special Pyrex Erlenmeyer flask (*Stoll egg-counting flask*), with etched markings at the 56 cc. and 60 cc. levels, are placed in sequence 56 cc. of decinormal NaOH and 4 cc of feces. Several glass beads are added, the flask closed with a

must be used, for the larger amount, 100, in order to convert the count into eggs per gram of formed feces

Faust and Khaw (1926, 1927) found that fecal specimens over a period of ten to fourteen days are desirable in order to obtain an accurate daily average, and that much greater dependence can be placed on average daily output of eggs than on eggs per gram of feces, since the consistency of the specimen varies too widely to permit of accurate estimate of its water content

The Stoll technic has been employed in conjunction with worm-counts in *Necator*, *Ancylostoma*, *Ascaris*, *Clonorchis* and *Fasciolopsis* infections in order to determine the egg-laying capacity of these species of worms per unit of time or per unit of formed fecal output The following figures may be considered as relatively accurate estimates for these worms: *Necator*, ca 9000 eggs per female *per diem* (Stoll, 1923); *Ancylostoma*, several times that of *Necator* (Sweet, 1924, Cort, Stoll and Grant,

tic species such as *Clonorchis* and *Fasciolopsis*, this product constitutes the estimated number of worms in the infection; for unisexual species, such as *Ascaris* and hookworms, *it is the estimate for females only and the total number of worms may* roughly be reckoned as twice that number, since the number of males and females is usually about equal.

9 **Beaver's Direct Smear Egg-count Technic.**—The method of making egg counts by direct smear is based on the observations that eggs of hookworms, and probably those of other species which inhabit the small intestine or upper colon, have random distribution in the stool, and that any series of direct smears of equal density taken from the same stool contain equal quantities of fecal solids and statistically equal numbers of eggs. A method of making uniform smears has been devised and the factor for converting eggs per slide to eggs per cc of formed stool has been determined for the type of smear which is regarded tentatively as being of ideal density This involves the use of photo-electric type of light meter which is adapted to measuring the turbidity of the fecal smear A wooden block 18 mm. in thickness and of any convenient diameter is fitted to the light meter's window and a 16 mm hole is drilled into the center of the block. This serves as a platform for the microscope slide on which the smear is made and provides a mask which reduces the window to a convenient size for preparing and spreading the smear An electric lamp is suspended directly over the reduced window and made adjustable so that arbitrary whole number readings can be obtained.

After the apparatus is assembled the procedure is as follows:

(a) Place a clean microscope slide on the platform and adjust the light to give a whole number reading with adequate working space between the meter and the lamp.

(b) Place one drop (0.045—0.050 cc.) of water or physiological saline on the slide over the window.

(c) With a wooden applicator take at random from the stool a small fleck of

into the smear are removed before the second reading is made so that the final smear contains pure feces only and nothing is present to prop the coverglass.

(d) Add coverglass and tap lightly to level it and spread the smear evenly to the coverglass edges.

(e) Count the eggs in the entire smear including any that may be outside the coverglass and record as eggs per slide.

For most purposes it is not necessary to interpret direct smear counts in terms of eggs per cc. of feces. For rough comparison with dilution egg counts, counts by direct smear should be multiplied by 300. *No correction in direct smear counts is necessary for stools of diverse consistencies.* However, standard smear counts multiplied by 300 give counts comparable with dilution egg counts corrected to the formed stool basis and do not actually give eggs per cc. when made on mushy or diarrheic stools. The direct smear method, therefore, can not be used to determine the total daily output of eggs if stools are not formed. On the other hand, *it offers the advantage of allowing direct interpretation in terms of worm burden without correction for stool consistency.* It has been determined that each egg on the standard direct ... *Necator americanus*. It must be emp... *for worms per egg) give* ...

For reliable comparison ... investigations it is necessary to have accurate calibration of the light meter assembly. This problem is discussed in detail in the original publication (Beaver, 1949).

10. **Caldwell and Caldwell Egg-count Technic** (1926).—In this technic antiformin and sugar solution are substituted for the decinormal NaOH. The containing tube or flask is calibrated to the 40 cc mark

... gar to 1000 cc. of tap ... introduced and the mixture thoroughly stirred. With a capillary pipette 0.1 cc. of suspension is drawn up from the bottom of the container, spread on a microscopic slide without a cover-glass and the eggs counted. To convert to eggs *per* gram of feces, the ...

The ac...

solution ...

cover-glass, and stays in position on the slide.

B. Recovery of Helminth Eggs from Soil.—For epidemiological surveys, in which it is desirable to determine the pollution of the soil with eggs of *Ascaris* and *Trichocephalus*, a generous sample of suspected soil is scraped from the surface layer, brought to the laboratory and treated by the Spindler (1929) or Headlee (1936) adaptation ... (1926) technic. A representative 5- to 10-Gm. portio... with 10 cc. of 30 pe... quently and thoroughly stirred to separate eggs from the soil particles

tubes are filled with a sodium dichromate solution (sp. gr. 1 35), thoroughly shaken

minute, the supernatant fluid is pipetted off and the sediment transferred to one or more broad fecal slides (37 x 75 mm) and examined

C. Concentration of Embryos and Larvæ.—The methods employed for concentration of larvæ in blood and lymph, in feces, or in soil contaminated with feces containing eggs or larvæ, have the same ends in view as the concentration of eggs in feces, namely, the diagnosis of light infections and the saving of time.

Blood, Lymph and Chylous Urine.—*Thick Film Methods.*—These methods have already been described (*vide supra*.).

Centrifugalization.—Defibrinated and dehemoglobinized blood, or lymph or chylous urine, is concentrated by centrifugalizing for about one minute at 1000 or more revolutions per minute, the supernatant fluid decanted and the sediment examined for embryos or larvæ. These may be vitally stained or the film air-dried, fixed and permananently stained.

Knott (1939) has modified this technic as follows: 2 cc of blood are thoroughly shaken with 10 cc. of a 2 per cent solution of formaldehyde, centrifugalized for five minutes at 2,000 rpm., the supernatant fluid decanted and the sediment stained in bulk, then examined microscopically for microfilariæ.

For the quantitative estimation of microfilariæ in blood samples Brady and Lawton (1944) recommend the following procedure:

"Twenty cubic millimeters of blood are drawn up into a pipette such as is employed for the hemoglobin estimation by the acid hematin technique. After wiping the tip of the pipette with cotton, the volume of blood is expelled into the chamber of the Sedgwick-Rafter counting cell. This cell was designed for enumerating organisms in water and consists of a slide with a depression 0.1 cm. in depth and 2 x 5 cm. in area, thus capable of holding 1 cc. of fluid. One cc. of 0.1 N hydrochloric acid is added, the suspension stirred with a dissecting needle, and a cover slip applied without leaving an air bubble in the chamber. The microfilariæ settle rapidly to the bottom of the chamber and little focusing is thus required With the aid of a mechanical stage, the entire area of the chamber is examined with the use of a 15 or 25 mm. objective.

"The method permits the examination of quantities of blood up to 0.1 cc., obviates the possibility of loss of microfilariæ in the test sample, and requires only a single piece of equipment. The only disadvantage encountered is that objectives providing magnification higher than 8 mm. cannot be used because of the thickness of the preparation."

Feces or Soil.—Larvæ in the feces, as for example hookworm or *Strongyloides*, may be diagnosed from unconcentrated fecal films, but centrifugalization, in the same manner as has been described for embryos or larvæ in the blood, lymph or urine, is usually indicated wherever there is a suspicion of these infections being present. For *Strongyloides* larvæ the zinc sulfate centrifugal floatation technic is particularly satisfactory (*Vide supra*). Another technic for *Strongyloides*, which has much to recommend it, consists (1) in the culture of the fecal sample in a covered Petri dish or glass bottle with a metal cap, and the recovery of the larvæ from the water of condensation on the underside of the cover, or (2) in the use of the Baermann apparatus.

sample is thoroughly mixed with an equal amount of sterile sand or animal charcoal, and placed on a circle of filter paper in a Petri dish (preferably of unglazed porcelain)

or in a stender jar. The container is covered with a glass lid, so that the water of condensation collects on the under side of the lid. In the course of several hours to a few days, depending on the species and the state of development at the time of culturing, the majority of the larvæ will be found to have collected in the water of condensation, and may be removed to a microscopic slide and examined. By this culture method practically the entire number of larvæ in the sample can be drawn off with the Baermann apparatus. (See below.)

Eggs of *Ascaris*, *Trichocephalus* and other nematode species which require several weeks for development to the fully embryonated stage may be placed on moistened circles of filter paper in covered Petri dishes. Development may be accelerated by keeping the culture in contact with a 2 per cent solution of formaldehyde. This solution must be thoroughly washed off before the embryonated larvæ are used for experimental feedings.

Eggs of *Schistosoma* species are fully embryonated on being passed in feces or urine and require only a dilution of the medium with tap water to secure hatching. This can be effected in the case of a fecal specimen by washing the specimen, allowing the eggs to settle, decanting the supernatant fluid and repeating the process until all of the lighter débris has been removed; or, in the case of urine, by simply diluting the specimen with 10 or more parts of water. The eggs usually hatch over night and the miracidia are found swimming about in the water next morning. The miracidia of *S. japonicum* collect in the uppermost portion of the water, as do the active miracidia of *S. mansoni* (Faust and Hoffman, 1934); those of *S. hæmatobium* are equally distributed throughout the medium. Faust and Meleney (1924) advocated this hatching technic as a simple method for determining the presence of small numbers of *Schistosoma japonicum* eggs in fecal samples.

Eggs of *Clonorchis*, *Opisthorchis*, *Metagonimus*, *Heterophyes* and *Dicrocœlium*, as well as those of *Tænia*, *Dipylidium* and *Hymenolepis* species, although fully embryonated when recovered from the feces, apparently hatch normally only after they have been ingested by the suitable intermediate host. Eggs of *Fasciola*, *Fasciolopsis*, echinostome species, *Paragonimus* and *Diphyllobothrium*, after being evacuated in the feces, mature in water. Development takes place most rapidly and the best yields of fully embryonated eggs are secured in shallow cultures at temperatures ranging from 20° C. to 30° C. Eggs of these species at the bottom of deep cultures develop very poorly. The available oxygen supply is apparently an important factor governing their development.

The Baermann Apparatus and Its Use.—This apparatus was originally devised for the isolation of hookworm larvæ from the soil. It is equally applicable for use in extracting other nematode larvæ from the soil, as well as nematode larvæ from the feces and larvæ hatched from eggs in cultured feces. The technic depends on the principle that a large proportion of nematode larvæ will migrate out of soil into water ... which is brought in contact with the
lower s...
placed ...
pinch-...
mesh b...
7.5 cm. is lined with coarse cloth and fitted into the funnel. The sample ... examined is comminuted and is then placed in the wire basket; the height of the ... has been ... introduced into the funnel, ... If a ... ween
piece of ice is then placed on top of ... o the
top and bottom will be greater and the movement of the larvæ downwards ... water will be more rapid. Usually within ten or fifteen minutes they will be observed migrating into the stem of the funnel. After about one hour the maximum number has collected in the lower part of the stem. The clamp is opened and about

50 cc of the water are run off into a centrifuge tube The draw-off is then centrifugalized, the supernatant water pipetted off and the sediment spread on a fecal slide for examination. Finely particulate soils may require a longer period of time for the migration of the larvæ.

If too much of the soil particles is present in the run-off, it may be necessary to utilize a small Baermann apparatus for a more careful separation of larvæ from these particles It is also sometimes necessary to repeat the process once or twice in order to obtain the maximum yield. This technic for the culture of the eggs to the hatching stage may be used as a substitute for either the Lane direct centrifugal

cation of the Baermann technic consists in providing a method for the accurate determination of the numbers of larvæ in the soil.

7 SEROLOGICAL DIAGNOSIS OF HELMINTHIC INFECTIONS

It is desirable wherever possible to diagnose helminthic infections from the worms themselves or their reproductive products, eggs, embryos and larvæ Under certain conditions, however, this is impossible except at operation or necropsy. In case direct diagnostic evidence cannot be obtained, sero-diagnostic methods may at times be utilized to advantage, in order to provide evidence of infection.

Serological and related reactions depend on the development in the body of a host-organism of specific antagonistic powers to an invading organism. In helminthic infections those species of worms which are intimately associated with the host tissues, so that their by-products become diffused throughout the body, are the ones which are most readily diagnosed by serological methods. Thus, the species of *Schistosoma*, *Echinococcus* and *Trichinella* give a positive serological test in a very high percentage of cases, while certain helminths of the intestinal tract, as well as certain of the trematodes resident in the biliary passages, give negative or uncertain tests. In the case of *Ascaris lumbricoides*, the worm need not be an actual parasite to provide a positive reaction, since emanations of this worm, as well as of the related species, *A. megalocephala*, have been found to sensitize certain persons handling or examining such specimens, or even those who are in environments having relatively large numbers of infected individuals. There is no unanimity of opinion as to the nature of the by-product of the helminth which is responsible for the sensitization, but most workers believe that group reactions are produced by a *gamma*-globulin, while species-specific reactions are due to polysaccharides. Thus, antigens prepared from generically or even less directly related parasites may serve for group reactions, while those which are purified will provide more convincing evidence of a specific etiological agent in the host.

The four types of reaction which have been obtained in the case of one or more of the human helminths are: (1) complement-fixation (= complement deviation of N. H. Fairley), (2) flocculation and precipitin reaction, (3) intradermal reaction and (4) precipitation.

1 **Complement-fixation.**—This test has been employed in practical diagnosis with positive results for the schistosomiases, paragonimiasis, hydatid cyst, and trichinosis. It has also been utilized in fascioliasis,

tæniasis and onchocercosis. Le Bas (1924) has found it negative in *Diphyllobothrium latum* infection and the present author has obtained negative results in clonorchiasis. The technic is on the whole similar to that of the Wassermann test for syphilis, although the antigen must be either species-specific or group-specific.

Bozicevich, Hoyen and Walston (1947) state that the complement-fixation test is frequently unreliable, due mainly to the anti-complementary effect of the antigen. They present a method from Wadsworth (1927) adapted to protozoan and helminthic infections. "Complement titer is determined on the basis of that amount which will give 50 per cent hemolysis when compared to the color standard." Interested workers should consult the original paper for technical details.

harboring either of these two species of blood flukes. Similar reciprocal use of

Both Yoshimoto

with 4 parts of physiological

per cent NaCl solution. If

stock solution remains potent for two months or more.

If antigen is prepared from infected snail hosts it is desirable to run parallel tests with extract of uninfected snails of the same species. If adult schistosomes are utilized as the source of antigen this precaution is obviated.

in an "alcoholic extract" of macer-

antiserum is prepared from serum of patients, inactivated for

C. and used undiluted; *complement* is fresh guinea-pig's serum, diluted just before using with 10 parts 0 85 per cent NaCl solution; *hemolysin* is inactivated serum of rabbits that have received at intervals of seven days, 3 to 4 intravenous injections

blood corpuscles in 0.85 per cent

freshly diluted co

hour in a water-b

gether with 1 cc.

tubes are placed in the water-bath again for two hours,

until next day, when readings are taken.

Fairley's Technic.—Antigen consists in the "alcoholic extract" of macerated snails infected with *Schistosoma hæmatobium* or *S. mansoni*, stored for twenty-four hours at 37° C., then filtered and the filtrate evaporated at 45° C. by means of an exhaust pump, the residue being dried, weighed and dissolved in 0.85 per cent NaCl solution (0.05 Gm. residue to 20 cc solution) *Antiserum*, *complement*, and *hemolysin* are prepared as in the Wassermann technic, and the subsequent procedure is similar to

that for the Wassermann reaction. Fairley (1919) stated that pooled positive sera collected from early cases of schistosomiasis fix 7 minimum hemolytic doses of complement over and above that fixed by pooled negative sera in the presence of specific antigen, while in the older, more chronic cases, this excess fixation amounts to about 4 M. H. D. of complement Yoshimoto found the fresh sera of schistosomiasis japonica cases to be strongly positive, while non-specific sera were negative or only faintly positive with schistosomiasis antigen

Miyaji and Imai (1928) found that physiological saline extraction provides a greater number of known positives than alcoholic extraction. Complement fixation with the former type of antigen discovered some cases of *S. japonicum* infection in endemic areas of Japan when the stools were negative Andrews (1935) obtained about 66 per cent positive reaction in *S. japonicum* patients' sera from China and obtained no false positives in luetic patients or those infected with *Clonorchis sinensis*, *Fasciolopsis buski*, *Ascaris* and hookworm Both antigen prepared from infected

Williams (1947), in testing 560 Australian troops who had been exposed to *S. japonicum* infection on Leyte, P I in 1944–1945, utilized antigen prepared in 1927 by Fairley from snails infected with *S spindale* In one group of 169 individuals, all with positive reaction, 25 were negative by stool examination. Of 365 persons previously regarded as negative, 34 had positive tests, 27 had positive stools and 26 of the 27 were positive by both technics. No false positives were encountered in unexposed persons or in those with positive Wassermann sera

The complement-fixation reaction is particularly valuable in suspected cases of schistosomiasis (1) during the latter part of the incubation period before the eggs are produced, (2) in chronic cases in which the walls of the intestine and bladder have become so fibrosed that eggs cannot pass from the mesenteric veins or vesical plexus into the lumen of these organs, and (3) in unisexual infections, which may otherwise be diagnosed as "idiopathic splenomegaly"

Paragonimiasis.—The test, as worked out by Ando, is similar to that for schistosomiasis, the antigen being prepared by saline extraction of macerated adult *Paragonimus westermani*, taken from a human infection at biopsy, or from autopsy or experimental infections in reservoir hosts The serological test is particularly useful in suspected cases of non-pulmonary paragonimiasis, where the worms are lodged in deep foci, which do not permit the eggs to be evacuated in the excreta or through cutaneous lesions

fixation" It seems probable that eggs recovered from biliary drainage will be a more reliable test than complement fixation

Echinococcus Infection. In this infection antigen usually consists of hydatid fluid removed aseptically from previous human cases or from infected mammalian reservoir hosts, preferably from infection in sheep with viable scolices (N H Fairley, 1922), but Dennis (1937) has pointed out that optimum results can be obtained only with a purified antigen made from sterile hydatid protein Except in heavily endemic areas, it is frequently difficult to obtain fresh antigen. Purulent or turbid hydatid fluid cannot be used.

Dennis's Technic (1937) —Freshly aspirated, bacteriologically sterile, hydatid fluid from cysts of the liver and lungs of infected cattle and sheep constitutes the

source of the antigen. About one liter of the fluid is chilled, acidified by the addition

the ice-box over night to accelerate

peated centrifugalization and is next

It is then suspended in about 50 cc. of distilled water and 10 per cent sodium hydroxide added, drop by drop, until practically all of the protein is in solution. The insoluble residue is collected by centrifugalization and discarded. The solution is then chilled, the protein reprecipitated by the addition of 1 N glacial acetic acid and left in the ice-box over night. It is then recentrifugalized, washed free of acid and evaporated in a drying oven at 37° C. or over calcium chloride The dry precipitate is ground in a mortar and stored over calcium chloride in a desiccator. About 100 mgm. of purified antigen may be obtained for each liter of hydatid fluid.

olution is made up 1

ay be sterilized by

chloroform This

ution is diluted to make

a 1

Kolmer modification of the wassermann test (Kolmer and Boerner, 1933). This antigen is sensitive, specific, not anti-complementary and does not give false positive tests.

Tænia Saginata.—Meyer (1910) and Jerlov (1919) have obtained complement-fixation in persons harboring the beef tapeworm They prepared their antigen by ether-alcohol extraction from dried *Tænia* strobilæ. Siever's (1935) suggestion, that the antigen of the tænias is species-specific, requires confirmation.

Trichinosis.—For the complement-fixation test in this infection Strobel (1911) found that trichinized flesh digested in a culture chamber for twenty-four hours with caustic soda and antiformin, and later neutralized with hydrochloric acid and filtered, provides a reliable antigen which is potent for fourteen days if kept in a refrigerator Alcoholic extract of trichinized flesh is said to give a negative reaction, 0 4 cc. of the antiformin extract has given a consistently positive reaction when known cases of trichinized individuals were tested, whereas a negative reaction was obtained with serum from a Wassermann-positive case. In experimental animals Bachman (1929) found that antigen, prepared as for the precipitin test, does not become positive until the experimental animal has been infected for twenty-five days

Ascariasis.—Antigen may be prepared by extracting in physiological saline solution the macerated adult worms which have been evacuated from human or porcine infections, then filtering and desiccating the solute The fact that the serum of *Ascaris*-infected individuals gives a positive reaction is of little but academic interest in patients harboring female worms, since eggs are so readily obtained for diagnosis, but in purely male infections it may have a definite use However, unin-

infection.

found *O. volvulus* antigen much more sensitive than antigens prepared from other filarial worms.

2 **Precipitin Reaction.**—This is a delicate, specific test but requires careful reading by skilled serologists. It is particularly helpful in checking intradermal tests made on patients suspected of harboring hydatid cyst, *Cysticercus cellulosæ*, *Trichinella spiralis* and schistosomiasis When properly carried out it provides more accurate information on active infection than does the intradermal reaction.

The basic technic (as worked out by Sawitz, 1937, for trichinosis) is as follows Eight serological tests tubes (I-VIII) are set up in series Into the first six, 0 2 cc amounts of patients' serum are introduced A normal human serum in the same amount is placed in the seventh tube and infected rabbit's serum in the same amount is placed in the eighth tube In the same order the tubes are over-laid with the following solutions. I, 0 2 cc antigen, 1 to 100 in Coca's solution, II, 0 2 cc antigen, 1 to 200, III, 0.2 cc antigen, 1 to 400, IV, 0 2 cc antigen, 1 to 800; V, 0.2 cc. antigen, 1 to 1600; VI, 0.2 cc Coca's solution without the antigen, VII, 0 2 cc antigen, 1 to 100; VIII, 0.2 cc. antigen, 1 to 100 (The rabbit serum should have been previously tested and found to be positive by the same technic) Negative sera remain clear, while positive sera develop a white ring, within thirty minutes at the level of contact with the antigen, and the antigen usually becomes cloudy white Although this technic is less sensitive than the intradermal test for chronic cases of trichinosis (Hall, 1937), it detects both subclinical and clinical cases of the infection

For hydatid cysts Dennis (1937) recommends 1 to 1000, 1 to 10,000 and 1 to 50,000 dilution of his purified powdered antigen, *i e*, stock solution, 1 to 10 and 1 to 50 dilution of stock solution Constant volumes of antiserum are utilized. This test is stated to be absolutely specific

Echinococcus Infection.—This precipitin reaction, which has been particularly studied by Australian investigators, closely parallels the complement-fixation reaction In practice, fresh hydatid fluid is obtained aseptically from infected sheep. It is preserved by the addition of phenol solution and will remain stable for several months 0 4 cc of patient's fresh serum is added to an equal amount of the antigen in small agglutination tubes and allowed to stand for thirty-six hours at room temperature. In a serum with high precipitin-content (*e g*, high serum euglobulin) a precipitate forms in two or three hours Thick flocculation has been designated as + + +, fine precipitate with granules in suspension, + +, and microscopic granularity, +

Cysticercosis Cellulosæ —The reaction is carried out as in testing hydatid infec-

paragraph to this serological method Antigen is obtained from laboratory infected animals (rats, rabbits, guinea-pigs), from the lean meat of which the larvæ are obtained by peptic digest technic, then concentrated by centrifugalization and desiccated in a partial vacuum

Olivér Gonzalez (1941) has discovered that there are two types of antibody reaction in trichinosis, one which is anti-larval and one anti-adult The latter forms a precipitate *in vitro* around the mouth, vulva and anus of adult trichinæ, is detectable 15 days after infection, reaches its maximum about the 25th to 35th day and terminates on the 50th day The anti-larval type of antibody produces a precipitate around the mouth (but not the anus of the larva,) appears about the 30th day and reaches a maximum between the 45th and 60th day

Roth (1945, 1946) has developed a slide precipitin test which he states is more reliable than the orthodox test The procedure is as follows About 100 sterile living *T spiralis*, obtained by muscle digestion of laboratory hosts, are placed in a

sterile, hollow-ground slide in 0.5 cc. of patient's *serum to be tested*, and the preparation is then mounted with a coverglass. The slide is set in a moist chamb... incubated for 24 hours at 37° C. ...

the larvæ in positive sera. A pa... positive 10 to 20 days after symptoms first appear. It is claimed to be more delicate and more trustworthy than other serological tests for trichinosis.

Suessenguth and Kline (1944) have adapted the Kline test for syphilis to trichinosis. They report early, accurate diagnosis ... on the intradermal tes... The antigen titer ranged from 1:5,000 to 1:30,000. All sera showed precipitins varying in degree from + to ++++. In four persons previously known to have the infection the reaction ranged from equivocal to +++. For preparation of the antigen *vide infra* under "Intradermal Reaction."

Schistosomiasis.—Employing antigens prepared from cercariæ and adults of *S. mansoni* and testing 86 patients harboring this parasite, Olivér Gonzalez and Pratt (1944) obtained 93 per cent positive precipitin reactions and no false positives in persons having other parasites. The titer used ranged from 1:3,200 to 1:4,000.

3. **Intradermal Reaction.**—This test consists of the injection intradermally of extract of parasite tissue or of fluid elaborated by the parasite, or in placing desiccated powdered tissue of the parasite on the skin which has been previously scarified. In sensitized individuals there is an immediate local reaction, consisting of an erythematous wheal which rapidly increases in size and tends to extend by pseudopodial runners until it reaches a maximum size in fifteen to twenty minutes, and begins to fade within an hour. There is usually also a delayed reaction some hours later, consisting of an area of erythema and induration around the site of injection or application of the antigen

Like other allergy skin tests the intradermal reaction in helminthic infections is simple to carry out and relatively easy to interpret. It has the disadvantage, compared with the precipitin reaction, in providing no selection of individuals actively infected, since it usually tests positive for infections which have long since become quiescent or may have been removed by anthelmintic treatment or surgical intervention.

Echinococcus Infection.—*The Casoni Reaction.*—The phenomenon of skin sensitiveness in echinococcus-positive individuals was first noticed by Casoni (1911), who obtained a proportion of positive reactions in cases of hydatid infection. Testi and Zoli (1919) and Dew, Kellaway and Williams (1925) have refined the test and ...

...ated with

test on a suspected case,

and 0.2 cc. of the antigen ... amount of physiological saline solution is made several centimeters from the first

injection or on the opposite arm. The wheal formed by the control fades, while that produced by the hydatid fluid in positive cases develops almost immediately into the typical wheal characteristic of the reaction. The test is particularly valuable in preoperative cases and the reaction is immediately positive, even in infections where operation showed the cyst to be suppurative and degenerate. In the latter type, as well as in recurrent cases, delayed reactions and complement-fixation are commonly negative. In postoperative cured cases intense skin reactions, including the delayed reaction, are obtained up to sixteen years, possibly due to considerable leakage of hydatid fluid at the time of operation.

For use with the Dennis purified antigen (1937) a 1 to 10,000 dilution in neutral physiological salt solution is recommended.

Cysticercosis Cellulosæ.—Since this is a group-specific test, antigen may be obtained from fluid in the bladders of various species of cysticerci in domestic animals The technic is carried out as for suspected hydatid disease

necessary to use uninfected molluscan-tissue extract for the control.

Olivér Gonzalez and Pratt (1944), testing 96 persons infected with *S. mansoni*, obtained 100 per cent positive skin reactions and no false positives. These workers

1947). Alves and Blair (1946) state that cercarial antigen provides a higher degree of accuracy than routine microscopic examination of stools.

Wright, Bozicevich, Brady and Bauman (1947) failed to elicit any positive skin reactions in American military personnel exposed to schistosomiasis japonica on Leyte, P I late in 1944 and early in 1945, four to five months before the tests were conducted However, 22 of 28 natives chronically ill with the disease gave positive tests The antigen was prepared from adult *S mansoni* and was employed in a dilution of 1 1,000, dry weight basis This might suggest that the intradermal test in schistosomiasis does not develop until the infection becomes chronic.

Trichinosis. The intradermal test is a valuable aid for diagnosing infection with *Trichinella spiralis* It is particularly helpful in mild cases which have a history of vague symptoms The following adaptation of the Bachman technic (1928) was

the material being kept at 37° C for five to twelve hours and shaken from time to time The digest is then poured through six layers of cheese-cloth, diluted with an equal amount of water and allowed to stand in a graduate for two hours. The upper third of the liquid is drawn off and replaced with warm tap-water. This process is repeated six or eight times until the supernatant fluid is clear. The purified material is left in a sedimentation glass overnight and next morning is placed in a Petri dish, allowed to dry and then transferred to a beaker with ether to remove lipoids. After twenty-four hours the ether is removed from the top and the residue dried *in vacuo* over sulphuric acid for forty-eight hours. The dry yield is pulverized in a clean dry mortar and kept in sterile ampules or dissolved in Coca's or McCoy's solution, 1 to 100 parts by weight This latter constitutes the stock

solution. For intradermal tests it is diluted 1 to 50 to secure a 1 to 5000 dilution. This is kept on ice until used. In the test, 0.1 cc. of antigen is introduced intracutaneously on one forearm and an equal amount of the solution lacking the antigen is injected intracutaneously on [illegible] her clinical or subclinical in type) a [illegible] and the injected site, surrounded by [illegible] about 5 cm diameter. The reaction reaches its maximum [illegible]

[illegible] to supplement the intradermal test with a precipitin test (vide supra).

Roth (1946) reports that in two outbreaks of trichinosis in Sweden in 1944 the intradermal reaction with an antigen "prepared [illegible] rized, extracted [illegible] s," but failed in

[illegible] of the former gave positive reactions at the onset of symptoms and both groups showed as high a percentage of immediate type of reaction three weeks later as when tested three and nine weeks later.

Filariasis.—This is a group reaction, although more reliable and more delicate reactions occur if the antigen is prepared from filariæ of the same species as that which is suspected to be present in the patient to be tested Satisfactory results can be obtained from antigen prepared from adult worms or microfilariæ. Commonly antigen is prepared from the dog heart worm, *Dirofilaria immitis.* For testing *Wuchereria bancrofti* Taliaferro and Hoffman (1930) used 0 025 cc of standardized solution, but Fairley (1931), who confirmed this test, used 0.25 cc of a 0.1 per cent solution.

Bozicevich and Hutter (1944) have used a precise technic with *Dirofilaria immitis* antigen for testing infection with Bancroft's filaria (*W. bancrofti*). In preparation of the antigen living adult *D immitis* were obtained aseptically from the right ventricle of the infected dog, were washed in sterile physiological saline solution, then in sterile distilled water, then immediately placed in sterile test tubes and frozen with dry ice. The worms were then thawed, cut in small pieces, ground moist in a mortar, then dried in a desiccator and finally reground Extraction was carried out in physiological salt solution 1 to 100 parts by weight for twenty-four hours in the ice-box The material was then frozen and thawed twice, then incubated at 56° C. for four hours with occasional shaking. It was next centrifugalized at 15,000 r p m for fifteen minutes, fractionally sterilized at 56° C. for one hour and tested for bacterial sterility. Finally 0.03 per cent phenol was added for preservation. When this stock antigen was needed for intradermal tests it was diluted 1 to 8000 with physiological salt solution. In 25 prepatent cases of the infection, using 0 01 cc of the diluted antigen positive reaction was obtained in all cases in fifteen minutes [illegible] excess of the cont[illegible] with this dilution, [illegible] in the tested individual

Chandler, Milliken and Schuhardt (1930) used *Dirofilaria* antigen for *Loa loa* infection, while Rodhain and Dubois (1932) used adult *Onchocerca volvulus* and *Loa loa* extracts as antigen to test infection with these two filaria worms. The immediate reaction, characterized typically by a diffuse erythema, wheal formation and pseudopodial extensions, covering an area of not less than 2 cm, is used in reading the test, which has an accuracy of at least 90 per cent.

During the epidemic of Bancrofts' filariasis among American troops in the South

Pacific area serological and immunological tests were carried out on many hundreds of individuals who had early clinical manifestations of the disease before the parent worms had matured and were shedding microfilariæ. Antigen prepared from *Dirofilaria immitis* was employed by Huntington, Fogel, Eichold and Dickson (1944) and several other groups for intradermal tests, with an approximate 90 per cent positive diagnosis. More recently Wharton (1947) used similar antigen in skin-testing 215 exposed individuals in British Guiana. Employing the antigen in 1:100,000 dilution and with diluted negative dog's serum as a control, Wharton obtained 89.8 per cent positive reactions, 5.1 per cent negatives and 5.1 per cent which were equivocal. Of the 29 cases with elephantiasis 26 reacted positively, one was negative and one was sensitive to dog's serum.

Skin testing of individuals in the *Onchocerca*-endemic area in Guatemala by Bozicevich *et al* (1947) with antigens prepared from *D. immitis*, *Setaria equina*, *Litomosoides carinii* and *O. volvulus* demonstrated that the *O. volvulus* antigen was more sensitive and more specific than the others, while *D. immitis* came next in producing satisfactory results.

Ascariasis.—The test consists in placing a few drops of body fluid of *Ascaris lumbricoides* on a scarified area of the skin. In sensitized individuals there is an immediate local reaction, consisting of an erythematous wheal at the site of application, and frequently extensive lymphatic and systemic involvement. The more alarming symptoms disappear in the course of an hour or two but generalized edema may persist for some days. It is important to note that *Ascaris*-sensitization does not necessarily mean infection with *Ascaris* at the time of the test, but may be the result of a previous infection or, in the case of workers in a laboratory, merely contact with fresh or preserved worms (Ransom, Harrison and Couch, 1924).

Strongyloidiasis.—The application of powdered *Strongyloides* to a scarified area of the skin produces in a few minutes an urticarial wheal in animals positive for this worm, even in cases of very light infection which require culture methods for diagnosis (Fülleborn, 1926).

Brannon (1943) utilized as antigen washed filariform larvæ of *Strongyloides* obtained from cultured feces of a naturally infected chimpanzee. The larvæ were ground up with emery powder, and the antigen extracted in Coca's solution, dried to powder form, and then diluted 1:100 in Coca's solution. Similarly prepared antigens from hookworm larvæ and bacteria in the original fecal specimen served as controls. Approximately 4 million larvæ produced 15 to 25 mgm. of powdered antigen. The powder was dissolved in Coca's solution to make a dilution of 1:100, which was demonstrated to be bacteriologically sterile. An amount of 0.1 cc. of this dilution was then employed in making the intradermal tests, which were carried out on 25 individuals with chronic strongyloidiasis. All provided positive reactions, while all controls were negative except for one suffering from severe exfoliative dermatitis and one moribund individual (Brannon and Faust, 1949).

4. **Precipitation Reaction.**—This is a non-specific test due to the excess of serum euglobulin elaborated in the animal body in the presence of certain disease-producing organisms. In India and China it has been utilized as a presumptive test for cases of kala azar. It may be conducted as an aldehyde (formol-gel) test (Napier, 1922, 1943) or a precipitation reaction (Sia, 1921, 1924).

The Napier method is as follows. One drop of 40 per cent formaldehyde is added to 1 cc. of patient's blood serum in a test tube, after which the mixture is well shaken and is allowed to stand at room temperature. If the reaction is positive, within 3 to 30 minutes it becomes solid and opaque.

The Sia method is as follows. Twenty cubic millimeters of the patient's blood,

drawn into a Sahli hemoglobin pipette, is expelled into a small test-tube containing 0.6 cc. of distilled water and gently agitated until the two parts are mixed. The tube is observed at once and at intervals of fifteen minutes, up to one hour. An immediate clouding of the water indicates a positive test. Sedimentation of the flocculent precipitate within fifteen minutes indicates a ++++ reaction; within thirty minutes, a +++ reaction; within forty-five minutes, a ++ reaction; and in one hour or longer, a + reaction.

Faust and Meleney (1924) found this test positive in schistosomiasis japonica patients free of kala azar, while Faust, Jones and Hoffman (1934) obtained eight positive tests in eleven patients suffering from chronic schistosomiasis mansoni in Puerto Rico.

In seriological tests of 104 schistosomiasis cases on Leyte, P. I., Wright *et al.* (1947) obtained positive reactions in 77 3 per cent of 75 military personnel and all of 29 Filipino civilians (chronic cases). There were 11 of 70 individual not known to have schistosomiasis who gave positive tests. Lal (1924) and Khalil and Hassan (1932) have obtained positive findings in other cases of schistosomiasis.

CHAPTER XXXV

INTERMEDIATE AND RESERVOIR HOSTS INVOLVED IN HUMAN HELMINTHIC INFECTIONS

INTRODUCTION

Perusal of the foregoing sections of this volume will indicate the considerable number of invertebrate and vertebrate animals which serve as intermediate hosts of human helminthic infections. In some cases, as in some of the tapeworm and in many of the nematode infections, and also in the blood fluke infections, there is only one intermediate host. In other cases there are two successive intermediate hosts required before the organism is ready to enter the definitive host. In the former case, without exception, the intermediate host is always an invertebrate. In the latter case, the first intermediate host is always an invertebrate animal, but the second intermediate host is in some instances an invertebrate animal and in other instances a vertebrate. It has seemed desirable to collect the information regarding the respective intermediate hosts involved in these infections and present it in brief systematic form, so that the reader will have some idea of the taxonomic relationships of these hosts. In practically n

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have been provided to help the student, who is not familiar with the invertebrate groups, to recognize at least the family and in some cases the generic characteristics of these organisms. The vertebrate forms are so much more diversified that it has not seemed wise to provide similar illustrations for them

INVERTEBRATE INTERMEDIATE HOSTS

With rare exceptions (*i. e.*, species of Branchiobdellidae [oligochete annelids] which serve as first intermediate hosts of the kidney worm, *Dioctophyma renale*), the invertebrate animals serving as intermediate hosts of human helminths belong to two large phyla of the Animal Kingdom, the **Arthropoda** (insects and their allies) and the **Mollusca** (snails *et al.*).

I **The Arthropoda.**—The arthropods are bilaterally symmetrical Metazoa, with a well-developed "body cavity" (technically known as a hemocele), segmented

Subphylum **CRUSTACEA** Pennant, 1777. This group of invertebrates consists of forms having typically 2 pairs of preoral, antenniform appendages and at least 3 pairs of postoral appendages acting as jaws. They are chiefly aquatic and breathe

entirely through gills. The important intermediate hosts of human helminths belong to a single class, the **Eucrustacea** Kingsley, 1894.

Class **Eucrustacea**. Kingsley, 1894. This is a large group of small Crustacea, which are fresh-water or marine species, free-living or parasitic in habits, and are usually considered of economic importance because they constitute the essential food supply of many food fishes of man. There are five recognized subclasses, viz, **Brachiopoda** Lamarck, 1801, **Ostracoda** Latreille, 1802, **Copepoda** Latreille, 1802, **Cirripedia** Burmeister, 1834 and **Malacostraca** Latreille, 1802. Species which serve as intermediate hosts of human helminths belong to the **Copepoda** and **Malacostraca**.

Subclass **Copepoda** Latreille, 1831. These are forms in which the body lacks a carapace, they consist of both free-living and parasitic species, the former being elongate, segmented, and having cylindrical thoracic appendages; also possessing 1 pair of maxillæ and 4 to 5 pairs of biramous legs. Two orders, **Eucopepoda** Claus, 1875, and **Branchiura** Burmeister, 1834, are recognized. Only species of the former group have been found to harbor human helminth larvæ.

Order **EUCOPEPODA** Claus, 1875. Females of this group carry egg-sacs. Compound eyes are lacking Two families of the Eucopepoda are involved in human helminthic infections, namely the **Diaptomidæ** Sars, 1897, and the **Cyclopidæ** Burmeister, 1834.

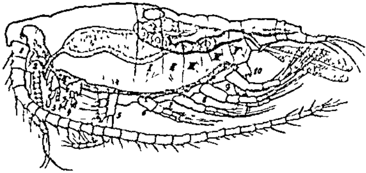

FIG. 287 – *Diaptomus castor* (After Kingsley, Courtesy of Henry Holt & Co)

Family *DIAPTOMIDÆ* Sars, 1897. The first pair of antennæ is long, commonly about as long as the body, and composed of 23 to 25 segments in females. The antennæ of the males are asymmetrical, the right being geniculate and modified as a grasping organ Several of the many recognized species of the type genus *Diaptomus* (Fig 287) have been found to serve as intermediate hosts of human tapeworms (*Diphyllobothrium latum, Drepanidotænia lanceolata*). (*Vide* p 262 and p 298)

Family *CYCLOPIDÆ* Burmeister, 1934. The first pair of antennæ is 6- to 17-segmented, never being shorter than the cephalothorax. The antennæ of the males are symmetrically geniculate The fifth feet are rudimentary, 1 to 3 segmented The females carry two egg-sacs Classification of the genera and species of Cyclops is based primarily on the number of segments and setal characteristics of the antennæ of the females the structure of the furcal rami of the abdomen, and the

(*Vide* p. 270 and p 548)

Subclass **Malacostraca** Latreille, 1802 This is an extensive group of the larger Crustacea, which usually possess abdominal appendages. They typically have 20 segments, 5 cephalic, 8 thoracic and 7 abdominal, of which those of the thorax and

entirely through gills. The important intermediate hosts of human helminths belong to a single class, the **Eucrustacea** Kingsley, 1894.

Class **Eucrustacea** Kingsley, 1894. This is a large group of small Crustacea, which are fresh-water or marine species, free-living or parasitic in habits, and are usually considered of economic importance because they constitute the essential food supply of many food fishes of man. There are five recognized subclasses, viz., **Brachiopoda** Lamarck, 1801, **Ostracoda** Latreille, 1802, **Copepoda** Latreille, 1802, **Cirripedia** Burmeister, 1834 and **Malacostraca** Latreille, 1802. Species which serve as intermediate hosts of human helminths belong to the **Copepoda** and **Malacostraca.**

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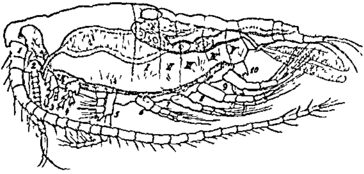

FIG. 287.—*Diaptomus castor* (After Kingsley, Courtesy of Henry Holt & Co.)

Family *DIAPTOMIDÆ* Sars, 1897. The first pair of antennæ is long, commonly about as long as the body, and composed of 23 to 25 segments in females. The antennæ of the males are asymmetrical, the right being geniculate and modified as *a grasping organ. Several of the many recognized species of the type genus Diaptomus* (Fig. 287) have been found to serve as intermediate hosts of human tapeworms (*Diphyllobothrium latum, Drepanidotænia lanceolata*) (*Vide* p. 262 and p. 298.)

Family *CYCLOPIDÆ* Burmeister, 1934. The first pair of antennæ is 6- to 17-segmented, never being shorter than the cephalothorax. The antennæ of the males are symmetrically geniculate. The fifth feet are rudimentary, 1 to 3 segmented. The females carry two egg-sacs. Classification of the genera and species of Cyclops is based primarily on the number of segments and setal characteristics of the *antennæ of the females, the structure of the furcal rami of the abdomen, and the* ... (Fig. 288). The genus *Mesocyclops* is the necessary first ... the genus

Subclass **Malacostraca** Latreille, 1802. This is an extensive group of the larger Crustacea, which usually possess abdominal appendages. They typically have 20 segments, 5 cephalic, 8 thoracic and 7 abdominal, of which those of the thorax and

abdomen are distinct. There are typically 19 pairs of appendages (5 cephalic, 8 thoracic and 6 abdominal). The division **Eucarida** Calman, 1904 contains the

Order **DECAPODA** Latreille, 1802, which is characterized by having a carapace covering all of the thorax, and includes all of the species of the group which are involved as intermediate hosts of human helminths. The species are commonly referred to as crayfishes and crabs In endemic areas in the Orient they live in more or less close association with the molluscan first intermediate host of *Paragonimus westermani* The cercariæ of the fluke encyst in the soft tissues of the crustacean, including the gills, liver and muscles. Mammalian infection is contracted almost exclusively from eating the raw or processed, but uncooked, tissues of the crustacean host

The crayfishes and lobsters belong to the

Tribe Astacidea Dana, 1852, and are

portion behind the thorax. They are grouped in two families.

Family *HOMARIDÆ* Bate, 1888 This group contains the lobsters, which are marine forms and do not harbor human helminthic infections

Family *ASTACIDÆ* Dana, 1852 (syn. *POTAMOBIIDÆ* Huxley, 1880) This group contains the crayfishes which are fresh-water forms. Two species of the type genus *Astacus* are involved as second intermediate hosts in *Paragonimus westermani* infection in Japan and Korea (*Vide* p 237.) Several species of the genus *Cambarus* have been found naturally infected with the metacercariæ of *P. kellicotti* in North America (*Vide* p 239)

The crabs belong to the

Tribe Brachyura Leach, 1813, and are characterized by having a flat body, a short abdomen, tail usually bent under the thorax, and a carapace fused with the epistome The fresh-water species involved in *Paragonimus westermani* infection belong to the families **Potamonidæ** Ortmann, 1896 and **Grapsidæ** Dana, 1851

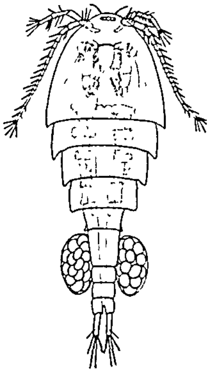

FIG. 288 — *Macrocyclops fuscus* (= *Cyclops coronatus* auct.), female dorsal view (Original.)

Family *POTAMONIDÆ* Ortmann, 1896 These are fresh-water or at times brackish-water crabs with a highly-developed and swollen branchial region, and usually with a squarish body Several species of the genera *Potamon* (subgenera *Potamon* and *Geothelphusa*) and *Parathelphusa* in the Sino-Japanese areas, and one species of *Pseudothelphusa* in Venezuela have been incriminated as second intermediate hosts of *P westermani* (*Vide* p 237)

Family *GRAPSIDÆ* Dana, 1851 These are fresh-water crabs having straight or only slightly arched sides The shape of the body is squarish or squarish-ovoidal Species of the genera *Eriocheir* and *Sesarma* have been incriminated as second intermediate hosts of *P westermani* in Japan (*Vide* p 237)

Class **Insecta** Linnæus, 1758 This group contains those arthropods which have three pairs of thoracic legs and usually two pairs of wings on the thorax, which

is composed of three segments, the prothorax, mesothorax and metathorax. They breathe by means of tracheæ The abdomen is composed typically of ten segments, of which the terminal one is modified for sexual purposes.

Order **DIPTERA** Linnæus, 1758. (Flies) The species of this order haveone pair of transparent wings and a pair of rudimentary wings (halteres or balancers). The mouth parts are adapted to piercing and/or to sucking. The metamorphosis is complete Of the three suborders, intermediate hosts of human helminths all belong to the

Suborder **Orthorrhapha.** The flies of this group lack a lunula or ptilinum The larvæ have a distinct head. The pupæ are obtectate. The imagos (adults) escape from the pupal cases through a T-shaped opening Most of the species of interest to students of human helminthology belong to the section **Nematocera,** but at least one species of the section **Brachycera** is also involved as an intermediate host of helminthic infections.

Section N*EMATOCERA Latreille, 1825. These forms have long antennæ, composed* of more than 6 segments, with all but the first two proximal ones similar. There is no arista. The discal cell of the wing is usually absent and the anal cell widely open at the margin. Three families of this group are involved in human helminthic infections, the **Culicidæ**, the **Chironomidæ** and the **Simuliidæ.**

Family *CULICIDÆ* Stephens, 1829. (Mosquitoes) These species have a long piercing proboscis and a body more or less clothed with scales or hairs. The *antennæ are provided with hairs in whorls, which are dense in the males and scanty* in the females. The wings have six or seven longitudinal veins, with two distinct fork cells but never with two distinct anal veins or a discal cell. The costa passes around the wing and is clothed with a fringe of scales There are two recognized tribes of the subfamily **Culicinæ** Theobald, 1901, which concern *helminthologists*, the **Anophelini** and the **Culicini.**

Tribe ANOPHELINI. These mosquitoes have the palps of both sexes as long as the proboscis, the terminal joints of the male palpi often being thickened. The apical joint terminates bluntly. The thorax is elongate and cylindrical, rarely rounded The posterior (free) edge of the scutellum is evenly rounded The abdomen is not densely invested with overlapping scales. The larvæ lack an air-siphon but have a conspicuous stigmal plate.

of the abdominal segments.

surface film When feeding,

Many species of the type genus *Anopheles* are involved as intermediate ... human filarial worms (*Wuchereria bancrofti* and *W. malayi*) (*Vide* p 508 and p 523.)

Tribe CULICINI In these mosquitoes the palps of the females are shorter than ... while those of the males are usually as long as, or much longer than,

distinct.

ncrofti and ...

Family *CHIRONOMIDÆ* Westwood, 1840. (Midges) The members of this very large family are small to medium-sized flies, with a small head, often concealed ... palps with 2 to 5 segments, and antennæ consisting ... margin ... re fre-

quently forked. The early stages of the life cycle are passed in water or mud. Two species, *Culicoides austeni* (Fig. 289) and *C. grahami*, are of importance as known intermediate hosts of *Acanthocheilonema perstans* in Africa, and *C. furens* as the known intermediate host of *Mansonella ozzardi* in the Caribbean area. (*Vide* p. 534 and p. 537.)

Family *SIMULIIDÆ* Latreille, 1804 (Gnats, black-flies or buffalo-flies.) The members of this small family are small, robust, hump-backed flies, with short

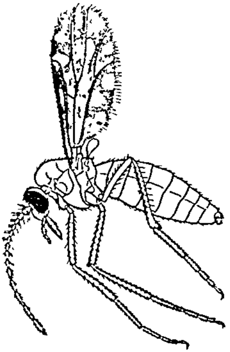

FIG. 289. *Culicoides austeni*, intermediate host of *A. perstans* in Africa, lateral view. (After Jobling in Sharp, Trans. Royal Soc. Trop. Med. Hyg.)

FIG. 290. *Simulium damnosum*, important intermediate host of *Onchocerca volvulus* in Africa, dorsal view. (After Carter in Byam and Archibald, Practice of Medicine in the Tropics.)

straight antennæ, consisting of 11 joints and lacking long hairs. The palps are small and incurved. The wings are broad and relatively large, and the legs are stout and large. Species of the genus *Simulium* are important as intermediate hosts of the human filarial worm, *Onchocerca volvulus*, in Africa (Fig. 290), Guatemala and Mexico. (*Vide* p. 527.)

Section BRACHYCERA HOMODACTYLA Macquart, 1834. Members of this group are characterized by having short antennæ with dissimilar joints. The important

family **Tabanidæ** is of great economic importance. The species of this family are commonly spoken of as "horse flies" or "gad flies."

Family *TABANIDÆ* Leach, 1819. These species are usually thick-set, bulky flies, with a head as wide as, or wider than, the thorax, convex in front ... large, brilliantly colo... y e ... l ... probably

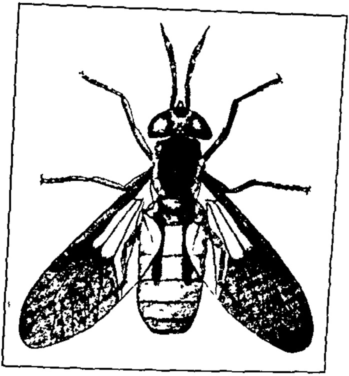

Fig. 291.—*Chrysops dimidiatus*, the mango fly, important intermediate host of *Loa loa* in Africa, dorsal view (After Grünberg in Martini, Text-book of Medical Entomology)

Order **SIPHONAPTERA** Latreille, 1825. (Fleas) This order contains those insects which have laterally compressed bodies with distinctly separated thoracic rings. Wings are lacking except for two lateral, plate-like structures on the mesothorax and metathorax. The mouth parts are adapted to piercing the skin and sucking blood. The antennæ are 3-jointed and are carried in a groove on either side of the head Metamorphosis is complete. Of the several recognized families the **Pulicidæ, Dolichopsyllidæ** and **Hystrichopsyllidæ** serve as intermediate hosts of human helminths.

Family *PULICIDÆ* Stephens, 1829 These species have a small head with rounded top. The abdomen is never so swollen as to lose its original contour. The venter is provided with hairs. The abdominal tergites have a single row of setæ. Members of the family are never tissue parasites The following species are important as proven intermediate hosts of cestode infections of man:

Pulex irritans, the human flea (Fig. 292), commonly found on man, dogs, cats and, at times, rats, throughout the world, serves as the intermediate host of *Dipylidium caninum* and possibly also of *Hymenolepis diminuta; Ctenocephalides canis*, the dog flea (Fig. 293*A*), with a cosmopolitan distribution, is the intermediate host of *D caninum* and possibly of *H diminuta*, while the related species, *C. felis* (Fig

the rat flea of 295), is an im-

Family *DOLICHOPSYLLIDÆ* Oudemans, 1909 In this family the head of the male is flattened on top There are no spines on the head, but always a comb of

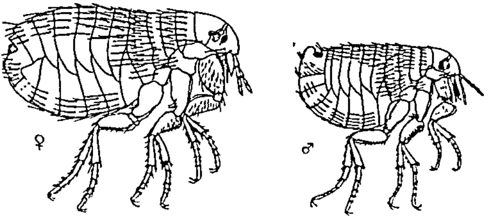

Fig 292 *Pulex irritans*; lateral views of female (left) and male (right) (After Castellani and Chalmers, Manual of Tropical Medicine)

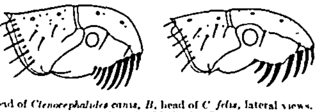

Fig 293 *A* head of *Ctenocephalides canis*, *B*, head of *C felis*, lateral views. (After Alcock, Entomology for Medical Officers)

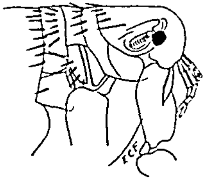

Fig 294 Head of *Xenopsylla cheopis* (Original)

spines on the pronotum There are three antepygidial bristles on each side of the female but frequently fewer in the male The abdominal tergites have 2 or more rows of setæ *Nosopsyllus fasciatus* (Fig 296), with an extensive distribution in Temperate Zones, is involved as an important intermediate host of *H diminuta*, while *Orchopeas wickhami* has been experimentally infected with this tapeworm in England (Oldham, 1931) (*Vide* p 297)

Family *HYSTRICHOPSYLLIDÆ* Baker, 1906. In this family the frons is separated from the occiput … the head to the base of each antenna … he species *Ctenopsyllus segnis* has bee … (Joyeux, 1920). (*Vide* p. 297.)

Order **ANOPLURA** Leach, 1815. (Sucking lice.) This order contains those insects with a proboscis consisting of a fused labrum and labium, armed with recurved hooklets, and containing a hollow extensile sucker formed by the mandibles and maxillæ, adapted for sucking. The antennæ are 5-jointed. The thorax is practically unsegmented and there are no wings. The legs have terminal claws

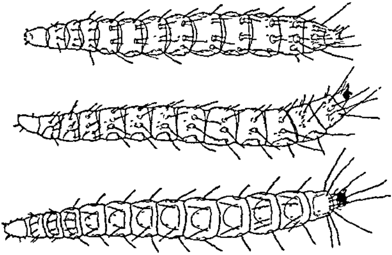

FIG. 295.—Larvæ of *X. cheopis*. (After Bacot and Ridewood in Martini, Text-book of Medical Entomology.)

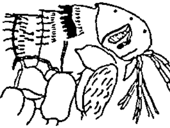

FIG. 296.—Head of *Nosopsyllus fasciatus;* lateral view. (After Alcock, Entomology for Medical Officers.)

adapted to clinging to the host. The last abdominal segment is rounded in the male and notched in the female. Metamorphosis is incomplete. These species must not be confused with the **Mallophaga**, which are chewing lice ectoparasitic on birds … Members of the *Anoplura*, particularly *Pediculus humanus*, … and have l … other …

Order **MALLOPHAGA** Nitzsch, 1818. (Chewing lice.) These insects are of small size and wingless, are provided with chewing mouth parts and with well-developed mandibles. The legs are flattened and end in one or two claws. One species of the family **Trichodectidæ** Burmeister, 1835, *Trichodectes canis*, the common dog louse, which is cosmopolitan in distribution, is believed to be an intermediate host of *Dipylidium caninum* or a closely related species of this genus. (Fig. 297.) (*Vide* p. 287.)

Order **LEPIDOPTERA** Linnæus, 1758 (Moths and butterflies) This order comprises those forms which have two pairs of membranous, expansive wings, clothed with scales. The mouth parts are adapted only to sucking Metamorphosis is complete. Several species of the suborder **Microlepidoptera** have been incriminated as intermediate hosts of *Hymenolepis diminuta*. The larval stage of the tapeworm is acquired by the larval lepidopteran, which has chewing mouth parts. Both the larval and adult lepidopteran may serve as passive transmitting agents of the parasite. The species found to harbor the larval stage of *H. diminuta* include: *Pyralis farinalis* (the "meal-worm"), *Aglossa dimidiata* and *Aphomia gularis* of the family **Pyralidæ**, *Tinea granella* and *T. pellionella* of the family **Tineidæ**. (*Vide* p. 296.)

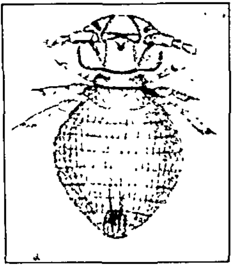

Fig. 297 *Trichodectes canis*, the dog louse, dorsal view. (After Piaget)

Order **ORTHOPTERA** Oliver, 1789 (?) (Grasshoppers, crickets, cockroaches, earwigs, etc) This order consists of forms having the first pair of wings leathery in consistency and forming a covering over the second pair, which are membranous The mouth parts are adapted to chewing There is no pupal stage.

The suborder **Saltatoria** contains those forms which have legs of unequal size, the hind femora being enlarged for leaping They comprise the grasshoppers, *locusts and crickets Several species of this group are larval hosts of gordiacean* worms, which are at times accidentally ingested by man

The suborder **Cursoria** contains those forms which have legs of approximately equal size and not adapted to leaping They comprise the cockroaches, praying insects and stick insects The cockroaches are important intermediate hosts of certain helminthic infections

Family *BLATTIDÆ* Stephens, 1829 (Cockroaches.) These species have a very large pronotum which often conceals the head Their broad coxæ cover the ventral surface of the thorax and the base of the abdomen The species of this family which have been found to serve as intermediate hosts and or mechanical vectors *of human helminths include*

Periplaneta americana (Fig 298), cosmopolitan in distribution, intermediate host of *Hymenolepis diminuta*, *Raillietina madagascariensis* (?), *Gongylonema pulchrum*, and *Moniliformis moniliformis*, and vectors of *Ascaris*, *Trichocephalus* and *Enterobius* eggs

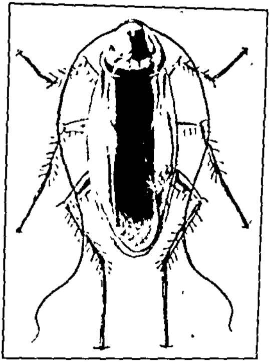

FIG. 298 —*Periplaneta americana*, the "American cockroach." (After Marlatt, U S Department of Agriculture)

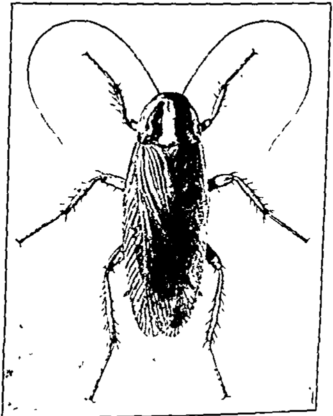

FIG. 299 —*Blatella germanica*, the "German cockroach" (After Terzi in Sambon, Journal of Tropical Medicine and Hygiene)

Blattella germanica (Fig. 299), cosmopolitan in distribution, intermediate host of [illegible] vectors of *Ascaris*, *Tricho-* [illegible]

[illegible] -mediate host of *M. moniliformis*, and probably a mechanical vector of several helminth eggs; *Dorylæa rhombifolia*, in Asia, Africa and Hawaii, mechanical vector of *Ascaris* and *Trichocephalus* eggs (*Vide* pp. 340, 373, 467.)

The suborder **Euplectoptera** (order **Dermaptera** of some authors) comprises elongate insects, having the forewings modified into very short, leathery tegumenta and having the caudal cerci unjointed and usually modified into horny forceps. They are commonly called "earwigs." One species, *Anisolabis annulipes*, is the intermediate host of *Hymenolepis diminuta*.

Order **COLEOPTERA** Linnæus, 1758 (Beetles.) These are insects which have the fore-wings modified into horny or leathery elytra, which almost always meet to form a straight mid-dorsal suture, and hind-wings, either membranous and folded beneath the elytra, reduced or wanting. The mouth parts are adapted to chewing. Metamorphosis is complete. The group is a very large one and comprises thousands of species. The larvæ of many species of beetles become infected with [illegible]

(?)

Series CLAVICORNIA (Family *TENEBRIONIDÆ* Leach, 1817). This is a very large family which is cosmopolitan in distribution, some species living in the ground, [illegible]

Akis spinosa, intermediate host of *Hymenolepis diminuta* (*Vide* p. 297);

Blaps appendiculata, intermediate host of *Gongylonema pulchrum* (*Vide* p. 485),

Blaps gigas and *B. mucronata* intermediate hosts of *Moniliformis moniliformis* (*Vide* p. 339);

Scaurus striatus, intermediate host of *H. diminuta* (*Vide* p. 297),

Tenebrio molitor and *T. obscurus*, intermediate hosts of *H. diminuta* (*Vide* p. 297),

Tribolium castaneum (vel *T. ferrugineum*), intermediate host of *H. diminuta* (*Vide* p. 297),

Ulosonia parvicornis, intermediate host of *H. diminuta* (*Vide* p. 297),

Omophlus rugosicollis (Family *ALLECULIDÆ*), intermediate host of *Macracanthorhynchus hirudinaceus* (*Vide* p. 337),

Series POLYFORMIA (Family *DERMESTIDÆ*)

Dermestes peruvianus and *D. vulpinus*, have been incriminated as intermediate hosts of *H. diminuta*. (*Vide* p. 297.)

Series PALPICORNIA (Family *HYDROPHILIDÆ*)

Tropisternus collaris has been incriminated as intermediate host of *M. hirudinaceus*. (*Vide* p. 337.)

Sphæridium sp. has been found to be an intermediate host of *Gongylonema pulchrum*. (*Vide* p. 485.)

Series CLAVICORNIA (Family *ANOBIIDÆ*)

Anobium paniceum has been incriminated as an intermediate host of *H. diminuta* (*Vide*, p. 297.)

Series LAMELLICORNIA (Family *SCARABÆIDÆ* Leach, 1817). This extremely large family comprises those species having highly differentiated antennæ of a lamellate, club type, body incapable of being rolled up, legs 5 jointed, the first pair

being sometimes wanting. The elytra usually fail to cover the abdomen. Th larvæ of a large portion of these species live in the ground, or feed on decaying vege tation or dung. The adults are frequently omnivorous. Species incriminated a intermediate hosts of helminths of man include.

Amphimallus solstitialis, intermediate host of *M. hirudinaceus;*
Anisoplia segetum, intermediate host of *M. hirudinaceus;*
Anomala vitis, intermediate host of *M. hirudinaceus;*
Aphodius distinctus, intermediate host of *H. diminuta,*
Aphodius fimetarius and related species of the genus, intermediate host of *G. pulchrum,*
Caccobius schreberi, intermediate host of *G. pulchrum,*
Cetonia aurata, intermediate host of *M. hirudinaceus,*
Diloboderus abderus, intermediate host of *M. hirudinaceus,*
Epicometis hirta, intermediate host of *M. hirudinaceus;*
Geotrupes stercosus, intermediate host of *H. diminuta;*
Gromphas lacordairei, intermediate host of *M. hirudinaceus,*
Melolontha melolontha, intermediate host of *M. hirudinaceus,*
Onthophagus taurus and other species of the genus, intermediate host of *G. pulchrum;*
Phanæus splendidulus, intermediate host of *M. hirudinaceus;*
Phyllophaga fervida, P. rugosa and *P. vehemens*, intermediate hosts of *M. hirudinaceus,*
Polyphylla fullo, intermediate host of *M. hirudinaceus;*
Scarabæus sacer, intermediate host of *M hirudinaceus;*
Strategus julianus, intermediate host of *M. hirudinaceus;*
Xylorycles satyrus, intermediate host of *M hirudinaceus* (*Vide* pp. 297, 337, 485.)

Class **DIPLOPODA** Latreille, 1802. This class comprises tracheate arthropods in which there is a head, bearing one pair of antennæ and jaws, and a trunk, made up of a number of similar segments, each of which, with the exception of the first three, bears two pairs of legs The genital apertures are situated towards the anterior end of the body. These arthropods are commonly called "millipedes" Species of the genus *Julus*, as well as *Fontaria virginiensis*, have been found to serve as intermediate hosts of *Hymenolepis diminuta* (*Vide* p 297.)

II. The Mollusca.—The molluscs (Phylum **Mollusca** Linnæus, 1758) are Metazoa, which have the common characteristics of being fleshy organisms lacking segmentation, of having a reduced celom or body cavity, and of having, as a rule, an exoskeleton which frequently takes the form of a shell. They include the snails, ... of the
...pods
...ity;
... man
... by
trematode parasites in their intermediate stage are ... it seems likely that bivalves fresh-water or amphibious snails, but in rare instances it seems likely that bivalves serve in this capacity. In general, the gastropod hosts belong to two groups, the ... forms which have an operculum, and those breathing by means of a
... on the form and characteristics of the
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Class **GASTROPODA** Cuvier, 1798. This group consists of forms with asymmetrical organization, with a well-developed head, usually bearing contractile tentacles, and with an external shell which is spirally coiled, at least in the larval stage. There are two subclasses, the **Streptoneura** and the **Euthyneura.**

Subclass **Streptoneura** Spengel, 1881. In this group the visceral nerve commissure is twisted into a figure "8." The species are usually diecious There are two orders of this subclass, the **Aspidobranchia** and the **Pectinobranchia.** The

Fig. 300

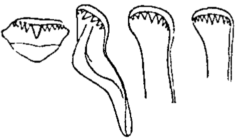

Fig. 301

Figs. 300 and 301 —Radula patterns of the family Melaniidæ Fig. 300, *Melania hainanensis* (After Walker in Faust and Khaw, Am. Jour. of Hygiene) Fig. 301, *Melanoides trigrina* (After Annandale, Prashad and Kemp, Records of the Indian Museum)

Order Pectinobranchia Cuvier, 1817 There are two suborders, the **Stenoglossa,** characterized by having a proboscis, a pallial siphon and a "poison gland," and the **Tænioglossa,** characterized by the absence of these organs. Only the latter group contains human fluke infections

Suborder **Tænioglossa** Troschel, 1866 There are two superfamilies, **Heteropoda,** with a laterally flattened foot and adapted to swimming, and the **Platypoda,** with a ventrally flattened foot and adapted to creeping.

Superfamily Platypoda. There are many families belonging to this superfamily. Certain of these contain species which serve as the intermediate hosts of human trematodes.

Family *MELANIIDÆ* Gray, 1840. (Fresh-water forms) The members of this group have a broad snout, hollowed out in front; separate tentacles, at the base of which are found the pedunculated eyes, a broad, short foot, provided with furrowed margins, a mantle, which is fringed or festooned, and single, leafletted gills, which are stationary. The shell, which is usually darkly colored, is dextrally wound, turriculated, usually imperforate, and often eroded at the summit, cleanly cut or sinuous at the base, and provided with a spirescent, horny operculum Radula patterns are illustrated in Figs 300 and 301. Species of two genera of this family,

viz., *Semisulcospira* and *Tarebia*, and possibly species of other genera of this family are necessary intermediate hosts of *Paragonimus westermani* and several species of heterophyid flukes. (*Vide* pp. 227, 229, 236.)

Family *CERITHIIDÆ* Fleming, 1828. (*Fresh-water forms.*) The members of this group have a broad, short, contractile rostrum and widely separated tentacles, with short penduncles on their outer aspects, bearing eyes. The radula is long. The shell is many whorled, turricated, frequently tuberculated or spinose. The operculum is horny, spiralled, with a central or sublateral nucleus. One species of this family, *Pironella conica*, is the first intermediate host of *Heterophyes heterophyes* in the lower Nile Valley. (*Vide* p. 224.)

Family *AMPULLARIIDÆ* D'Orbiny, 1842. (Fresh-water forms) The members of this group have a snout divided into two tentaculiform processes; two long tentacles with a pair of pedunculated eyes at their outer base; two cervical appendages, of which the left is modified into a siphon; a branchial chamber divided by a

Fig 302 —Radula pattern of the family Ampullariidæ. (Reprinted by permission from "Fresh-Water Biology" by Henry B Ward and the late George C. Whipple, published by John Wiley & Sons, Inc.)

Fig 303

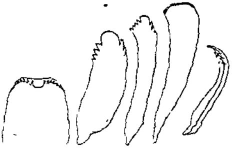

Fig 304.

Figs 303 and 304 —Radula patterns of the family Viviparidæ. (Fig. 303 reprinted by permission from "Fresh-Water Biology" by Henry B. Ward and the late George C Whipple, published by John Wiley & Sons, Inc ; Fig 304, after Walker in Faust and Khaw, Am Jour of Hygiene)

partition, with a single large monopectinate gill and a small rudimentary gill on the right and a "lung" on the left. The radula pattern is illustrated in Fig 302 Shell large, turbinate, umbilicate, provided with a large oval opening into which fits a horny operculum with excentric nucleus. Several species of *Pila* have been found to be second intermediate hosts of species of *Echinostoma* (*Vide* pp. 191–195) and *Ampullaria luteostoma* is reported to be the molluscan host of *Paragonimus* ... in Venezuela (*Vide* p 237)

... Brackish-water forms.) Animal operculate, ... One ... 37.) ... host of *Paragonim* ... ers ... 363 (Fresh-water forms) The snout ... ; the tentacles are elongate conical, with pedunculated eyes on the outer aspect. Shell of moderate to large size, dextral, turbinate, imperforate or subperforate. Operculum horny, strongly searred *on inner surface* The radula pattern is illustrated in Figs 303 and 304.

Species of this family which are reported as molluscan hosts of trematodes of human interest include: *Viviparus viviparus*, second intermediate host of *Echinostoma revolutum* (*vide* p. 194); and *Cleopatra bulimnoides* and *C. cyclostomoides*, intermediate hosts of *Gastrodiscus ægyptiacus*, Egypt. (*Vide* p. 170).

Family *RISSOIDÆ* H. and A. Adams, 1858. (Both fresh-water and salt-water forms.) The members of this group have a simple or transversely cleft foot; long

basal denticles. Only fresh-water forms are involved in human trematode infections Of the five or more subfamilies only the **Triculinæ**, the **Bithyniinæ** and the **Pomatiopsinæ** concern helminthologists

Subfamily *Triculinæ* Annandale, 1924. The shell of these species is conical, conidal or turricated and slender; the operculum is small, thin, horny and capable of being drawn into the interior of the shell The radula patterns are illustrated in Fig 305*A*, *B*, *C*. There are two closely related genera of this subfamily which serve as the intermediate host of the Oriental blood fluke. The shells of both types have a thickened peristome These forms are amphibious

FIG. 305—Radula patterns of the subfamily Triculinæ (family Rissoidæ). *A*, *Oncomelania hupensis*; *B*, *Oncomelania* (*Katayama*) *nosophora*; *C*, *Oncomelania* (*Katayama*) *formosana*. (*A*, original, *B*, *C*, after Annandale in Faust and Meleney, Am Jour. of Hygiene)

The species which are the molluscan hosts of *Schistosoma japonicum* include. *Oncomelania hupensis*, having prominent longitudinal ridges on the shell, the Yangtze Valley, China; *O. quadrasi*, Philippine Islands, *O nosophora*, having an elongate smooth shell, with eight whorls, Japan, and coastal China from Shanghai to Canton, *O. formosana*, having a shell somewhat shorter than *K. nosophora*, with less than seven whorls, lacking external sculpturing, Formosa (*Vide* p. 145)

The status of *O.* (*Katayama*) *fausti*, *O. fausti* var. *cantoni*, *O yaoi*, *O. tangi*, etc. of Bartsch (1925–1939) is unsettled until more careful study can be made of the relationships of these forms in China

Subfamily *Bithyniinæ* Stimpson, 1865 The shell of these species is ovate or subglobose, smooth to the naked eye or with spiral ridges; the operculum is thick and calcareous, wholly concentric or with a small central or subcentral spiral nucleus. The lips are sharp or more or less thickened and reflected The central tooth of the radula has several basal denticles The radula patterns are illustrated in Figs 306, 307 and 308

Species of *Parafossarulus*, *Bulimus* and *Alocinma* have been found to be first intermediate hosts of *Clonorchis sinensis* (*vide* p 214), and *Bulimus leachi* of *Opisthorchis felineus* in Prussia.

Subfamily *Pomatiopsinæ*. Members of this group have a foot divided by a transverse sulcus, and a very long snout The shell is elevated and turreted and the operculum is subspiral. The species are found near, but rarely in, fresh water.

Pomatiopsis lapidaria is the first intermediate host of *Paragonimus kellicotti*, U S A (*Vide* p 239.) This widely distributed snail is also a *potential host of Schistosoma japonicum*, as demonstrated by laboratory tests (Berry and Rue, 1948)

Subclass **Euthyneura** Spengel, 1881. In this group the visceral nerve loop lies beneath the intestinal canal and is consequently not affected by the torsion to which

that organ has been subjected. The aquatic members of this subclass all belong to the order **Pulmonata.**

Order PULMONATA Ehrenberg, 1931. These are air-breathing species, provided with a lung and breathing tube, and lacking gills and an operculum. They are divided into two suborders, the **Stylommatophora,** in which the eyes are borne on the extremities of retractile tentacles, and the **Basommatophora,** in which the eyes are situated at the base of contractile tentacles. Practically all species of this order involved in human helminthic infections belong to the second group.

ORDER STYLOMMATOPHORA Members of this group have four retractile tentacles, with eyes at the tip of the second pair Some species, as the slugs (family

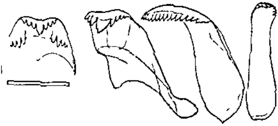

FIG. 306.

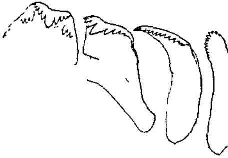

FIG 307.

FIG. 308.

FIGS. 306, 307 and 308 —Radula patterns of the subfamily Bithyninæ (family Rissoidæ) FIG 306, *Parafossarulus striatulus;* FIG 307, *Bulimus fuchsianus;* FIG 308, *Alocinma longicornis* (After Walker in Faust and Khaw, Am Jour. of Hygiene)

LIMACIDÆ), have only a concealed shell, while others, as the land snails belonging to the family *HELICIDÆ*, have a well-developed shell Several genera of the latter family have been incriminated as the intermediate host of *Dicrocœlium dendriticum*, namely *Abida, Cochlicella, Euomphalia, Helicella* and *Zebrina* (*vide* p. 204)

Order BASOMMATOPHORA Members of this group have a single pair of retractile tentacles. All species of medical importance belong to the superfamily LIMNOPHILOIDEA

Superfamily LIMNOPHILOIDEA (Menke, 1828) The members of this group are fresh-water forms, which usually come to the surface from time to time in order to breathe The following families are important in human trematode infections

Family *LYMNÆIDÆ* Brod, 1939 The shell of species of this family is ovoid or elongated, with a dextral spiral The animal is provided with three smooth jaws The radula patterns are illustrated in Figs. 309, 310, 311

Many species of this family belonging to the genera *Lymnæa* (*sensu stricto*), *Fossaria, Galba, Pseudosuccinea, Radix, Stagnicola,* etc. are intermediate hosts of *Fasciola hepatica, F. gigantica, Fascioloides magna,* dermatitis-producing schistosomes, echinostomes and other trematode parasites affecting man (*Vide* pp. 173, 191, 193, 194.)

Family *BULINIDÆ* Germain and Neveu-Lemaire, 1926. The shell of species of this family is sinistrally coiled, ovoid, globose or elongated, with a spire, either short or elongated, and more or less obtuse at the summit. The radula patterns are illustrated in Fig. 312 *A* and *B*. Two genera of the family, *Bulinus* and *Physopsis*, harbor species of *Schistosoma* and possibly other trematodes affecting man. (*Vide* pp. 110, 128, 161.)

Family *PHYSIDÆ*. The shell of species of this family is spiral, sinistrally coiled. The animal is sinistral and has slender, cylindrical tentacles. Several species of *Physa* (*sensu lato*) have been found to be first intermediate hosts of *Echinostoma revolutum* (*vide* p. 194) and molluscan hosts of certain dermatitis-producing schistosomes (*vide* p. 162).

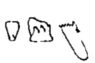

FIG. 309.

FIG. 310.

FIG. 311.

FIGS. 309, 310 and 311.—Radula patterns of the family Lymnæidæ. Fig. 309, *Lymnæa natalensis;* Fig. 310, *L. truncatula,* Fig. 311, *L. gedrosiana.* (Fig. 309, after Cawston, Journal of Tropical Medicine and Hygiene, Figs. 310 and 311, after Annandale and Rao, Records of the Indian Museum.)

A B

FIG. 312. Radula patterns of the family Bulinidæ. *A*, *Bulinus (Isidora) forskali*, *B*, *Physopsis africana*. (After Cawston, Journal of Tropical Medicine and Hygiene.)

Family *PLANORBIDÆ* H. and A. Adams, 1858 (?). The shell of species of this family is discoidal, sinistral, or superficially dextral, or spiral with a very low spire. The animal is sinistral and the tentacles are cylindrical. The shell of species of the subfamily **Planorbinæ**, the group which concerns medical zoölogists, is always discoidal. The radula patterns of three of these species are illustrated in Figs. 313, *A*, *B* and *C*.

Species of *Segmentina* and *Hippeutis* are necessary intermediate hosts of *Fasciolopsis buski* (*vide* p. 184), *Planorbis dufourii*, of *Schistosoma hæmatobium* in Portugal (*vide* p. 111), species of *P.* (*Biomphalaria*), of *S. mansoni* in Africa, and species of *Australorbis* and *Tropicorbis*, of *S. mansoni* in endemic foci in tropical America (*vide* p. 128). Moreover, *Indoplanorbis exustus* has been demonstrated to be the molluscan host *S. spindale* (*vide* p. 161) and a second intermediate host of *Echinostoma malayanum* (*vide* p. 193), species of *Gyraulus*, the first intermediate host of *E. ilocanum*, and species of *Helisoma*, *Segmentina* and *Planorbis* (*sensu lato*), of *E. revolutum* (*vide* p. 194).

Class **LAMELLIBRANCHIA** De Blainville, 1924. These molluscs are acephalous and are provided with two opposing valvate shells, which are united by a ligament. Several species of this class have been mentioned as harboring trematodes reported from man. These include species of *Corbicula* as second intermediate hosts of *Echinostoma lindoënse* and possibly *E. revolutum* (*vide* pp. 192 and 194), *Musculium* and possibly *Pisidium* and *Sphærium* of *E. revolutum*, *Cerithidia* of *Heterophyes heterophyes*, and possibly *Venus mercenaria* of *Himasthla muehlensi.*

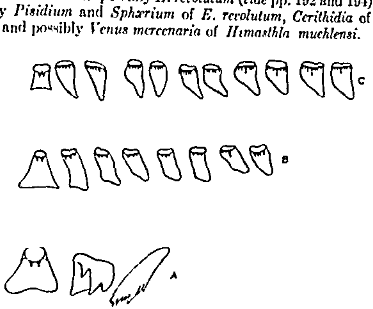

FIG. 313.—Radula patterns of the family Planorbidæ. *A*, *Planorbis* (*Biomphalaria*) *pfeifferi*; *B*, *Hippeutis umbilicatus*; *C*, *Segmentina calathus*. (*A*, after Cawston, Journal of Tropical Medicine and Hygiene. *B*, after Annandale, Prashad and Amin-Ud-Din. *C*, after Annandale and Prashad. Records of the Indian Museum.)

VERTEBRATE INTERMEDIATE HOSTS

Essentially all main groups of vertebrate animals are involved as intermediate hosts of human helminths. Fishes, frogs, snakes and birds are, in all recorded instances, second intermediate hosts. The mammals serving in this capacity are, in some cases, second intermediate hosts, in others, the sole intermediate hosts.

I. Fishes Serving as Intermediate Hosts.—With relatively few exceptions the fishes involved in human helminthic infections are all fresh-water species. A few

Helminths which have been found to exist in their larval stages in various fresh-water fishes consist of certain pseudophyllidean cestodes, all of the members of the opisthorchid and heterophyid trematodes of which the life cycles are known, and the nematode, *Dioctophyma renale*. Fishes which serve as second intermediate hosts

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lodgment in their subcutaneous and muscular tissues, of the cercarial stage of the fluke, which becomes encysted in the tissues. Although the species of fishes differ in different endemic areas, [illegible] the molluscan hosts of the [illegible] mollusc is liable to attack a [illegible] far been found to harbor the advanced larval stage of *Dioctophyma renale*, while the bullhead (*Ameiurus melas melas*) has been demonstrated to serve in this capacity in Michigan, U. S. A. Several species of fresh-water fishes have been incriminated as second intermediate hosts of *Gnathostoma spinigerum* (Prommas and Daengsvang, 1936; Daengsvang and Tansurat, 1938)

II. Frogs, Snakes and Birds.—Species of the genus *Diphyllobothrium* (subgenus *Spirometra*) may be found in the sparganum stage in several species of frogs and snakes Joyeux and Houdemer (1928) have found that certain birds may also harbor this stage of these tapeworms Encysted metacercariæ of *Echinostoma cinctorchis* have been discovered in the tissues of the tadpole of *Rana esculenta* in Japan. Chandler (1925) has found the advanced larval stage of *Gnathostoma spinigerum* in certain snakes, and Daengsvang and Tansurat (1938) reported infection in *Rana rugulosa*.

III. Mammals.—Mammals other than man occasionally harbor the sparganum stage of *Diphyllobothrium* (subgenus *Spirometra*). The pig serves as the intermediate host of *Tænia solium* and *Echinococcus granulosus;* the ox, as the intermediate host of *T saginata* and *E. granulosus*, the sheep, as the intermediate host of *Multiceps multiceps* and *E. granulosus*. The pig is also the important source of infection of *Trichinella spiralis* for man.

In all of these helminths of which vertebrates serve as intermediate hosts, with the exception of *Multiceps* and *Echinococcus*, man acquires the infection from consumption of the infected raw flesh of the vertebrate

Since the known number of species of these vertebrates is large and the number of potential intermediate hosts is even very much greater, it is not possible to list them here. Hosts which cannot be readily recognized by the student of helminthology should be referred to specialists for determination.

PLANTS AS VECTORS OF HUMAN HELMINTHIC INFECTIONS.

Plants which are involved in the dissemination of human helminthic infections fall into two categories, (1) those which harbor encysted larvæ of flukes, and (2) those which are parasitized by plant nematodes. In both cases the helminth is taken into the human body by consumption of the raw plant harboring the parasite. The first group consists of species of worms which are true parasites of the mammalian body, while the second group includes species which are only accidental or spurious parasites of the human intestinal tract.

To the first group of plants belong the various meadow and swamp grasses, and semi-aquatic plants such as cress, on which the cercariæ of *Fasciola hepatica, F. gigantica, Fasciolopsis buski, Dicrocælium dendriticum, Eurytrema pancreaticum* (?) and amphistomate flukes encyst, as well as the true aquatic species, such as the water-chestnut (*Eleocharis tuberosa*), the water-ling (*Trapa natans, T. bispinosa* and *T bicornis*) the water bamboo (*Zizania aquatica*), *Eichhornia crassipes, Salvinia natans, Lemna polyrhiza* and *Vallisneria*, the most common disseminators of *Fasciolopsis buski* Likewise, any of the meadow grasses in endemic foci may serve as vectors for the ensheathed infective-stage larvæ of *Hæmonchus contortus, Trichostrongylus* spp and related strongylate nematodes In the second group of plants there are included fleshy roots like the radish, turnips, etc , which are infected with [illegible] species like *Heterodera marioni*.

THE EXAMINATION OF INTERMEDIATE AND RESERVOIR HOSTS FOR LARVAL AND ADULT STAGES OF HUMAN HELMINTHS

A few brief suggestions relative to the technic and method employed in obtaining and examining the various groups of intermediate hosts for larval stages, and reservoir hosts for the adult stages, of helminths parasitic in man will probably be helpful to students of human helminthology who are contemplating the study of a particular problem in a given locality, either in an attempt to elucidate a life history or to secure epidemiological data. This information will be presented primarily according to the classification of the host involved, as presented in the preceding sections, rather than from that of the parasites.

Invertebrate Hosts.—Only larval stages of helminths parasitic in man are found in invertebrate hosts.

I. **Arthropoda.**—CRUSTACEA.—1. *Copepoda.*—In so far as is known, only free-living species (genera *Diaptomus* and *Cyclops sensu lato*) have thus far been incriminated as intermediate hosts of human helminths. These organisms are small creatures but are readily visible with the unaided eye, living in relatively quiet pools or puddles, either constituting permanent or temporary bodies of water. They are frequently associated with green algæ (*e. g.*, "pond scum"). They may be collected by sweeping suspected water with a muslin dip-net, allowing most of the water to drain out, pouring out the concentrated plankton into a large photographic developing tray and transferring to large jars or aquaria, from which they may be later picked out for examination. Individual copepods may be placed temporarily on a microscopic slide under a cover-glass to determine if they are naturally infected. The larvæ both of tapeworms (*Diphyllobothrium* spp and *Drepanidotænia lanceolata*) and of the Medina worm (*Dracunculus medinensis*), or *Dioctophyma renale*, if present, will be found in the hemal cavity of the copepod, and can be seen under low power of the microscope Since larvæ of other species of tapeworms are frequently harbored by these crustaceans, attention must be paid to the characteristics of the larval stages of the human tapeworms which develop in these hosts. In order to allow the larvæ to escape from *Cyclops* or *Diaptomus*, the posterior extremity of the abdomen may be dissected off, whereupon the larvæ will emerge from the opening and can be studied in greater detail In order to infect larvæ-free *Diaptomus* or *Cyclops* with *Diphyllobothrium*, fully-embryonated eggs or free-swimming, ciliated embryos are placed in a small container with the copepods The free-swimming embryos will be ingested by the copepods and in susceptible hosts will penetrate through the intestinal wall to the hemal cavity Heavily infected copepods are likely to die shortly after infection and will not allow the larvæ to mature Appropriate species of *Cyclops* may be infected with *Dracunculus* larvæ by placing the larvæ discharged by a female worm in the same medium The larvæ will break through the intestinal wall into the hemal cavity and become inactive in that location, remaining so until they come in contact with gastric juice.

2. *Decapoda* —Fresh-water crayfishes and crabs harbor only one type of human helminth larva, that of *Paragonimus* Only those species which live in association with appropriate species of molluscs in endemic areas of this infection are subject to suspicion. The animals may be caught by hand and placed temporarily in tin cans with perforated lids. For examination, the carapace of the animal is first dissected off. Then portions of the gills, or muscles from the appendages, are removed to shallow Petri dishes and any small spherical objects found are dissected out and examined under slight pressure with low power of the microscope. Unless these encysted larvæ conform to the type originally distinguished by Yokogawa (Fig 123) from other encysted fluke larvæ, they are not *Paragonimus* larvæ. If the gills are

found infected, the liver and muscles are likely to be even more heavily parasitized. These tissues may be examined by using a "trichina-press." However, convincing proof is not established until the encysted metacercariæ have been fed to *Paragonimus*-free susceptible mammals and the adult worms later recovered from these hosts.

INSECTA.—1. *Diptera.*—**Nematocera** and **Brachycera Homodactyla.** These forms, including mosquitoes, midges, gnats and *Chrysops*, are intermediate hosts of filariid worms. Wild flies may be caught (1) at the time they are taking a blood meal, by carefully placing over each one a test-tube and withdrawing it after the fly has released its hold on its victim, (2) by using the same technic in collecting them from the outside of a bed-net, (3) by collecting them from hiding places around buildings during the day, if they are nocturnal feeders, or (4) by sweeping with a fine muslin or bolting-cloth net any vegetation in which they are hiding.

For examination, the flies are first killed or anesthetized with chloroform, the legs and wings removed, and the body placed on a microscopic slide in a drop of physiological salt or Locke's solution. Under a dissecting microscope the head is [illegible]

contact with physiological Locke's solution. If this does not occur, the exoskeleton should be dissected off the thorax and the thoracic muscles carefully teased apart. [illegible] infections larvæ may be [illegible] hours after ingestion of [illegible] penetrating through the stomach wall. In attempting experimental infection of these several groups of flies, essentially the same technic of examination is employed, except that the early stages of development are looked for first. Frequently the nematoceran species suspected of harboring a filarial infection require to be fixed in alcohol or Carnoy's fluid, embedded, stained and sectioned, in order to determine the exact location of the larvæ in their bodies.

[illegible]

with them and for preservation removed with forceps to a chloroform bottle. For dissection, each flea is placed on a slide in a drop of saline solution. Larvæ of tapeworms, if present, will be found in the hemal cavity of the animal. They must be specifically differentiated from other tapeworm larvæ possibly harbored by these insects.

3. *Mallophaga.* The technic for examination of chewing lice is similar to that for *Siphonaptera*.

4. *Lepidoptera.* The larva or adult is first killed in chloroform vapor and dissected on a large microscope slide or in a small Petri dish. Larvæ of *Hymenolepis diminuta*, if present, will be found in the hemal cavity.

5. *Orthoptera.* The insect is first killed in chloroform vapor, placed in a shallow Petri dish, the legs, wings and mouth parts dissected off and the hemal cavity first opened up. Gordiacea, if present, will be found coiled in the hemal cavity. *Hymenolepis diminuta* and *Davainea* larvæ will also be in this locality. *Gongylonema* larvæ and those of *Moniliformis moniliformis* may be found encysted in the peritoneal wall but are more likely to be encysted in the thoracic muscles.

6. *Coleoptera.* The beetle is first killed in chloroform vapor, placed in a shallow Petri dish, the legs, wings and hard parts of the under side of the thorax and abdomen dissected off, and the hemal cavity then laid open. *Hymenolepis diminuta* larvæ, when present, are found in the hemal cavity; nematode and acanthocephalan larvæ are most likely to be found encysted in the thoracic muscles. Since beetles

harbor many species of larval nematodes, special care should be taken not to confuse larvæ of non-human species with those which may occur in man.

DIPLOPODA.—For examination of species of *Julus* and *Fontaria* for *Hymenolepis diminuta* the technic is similar to that for *Coleoptera*.

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because the number of species of trematodes of man is relatively small compared with the very large total of such organisms found in their intermediate stages in molluscs, the difficulty of differentiating the human forms during their molluscan phases is very great. Only the specialist in this group is prepared to attempt such differentiation, and he is at times baffled by the large number of forms which he encounters and the very few reliable characters which are available for the determination of species and even genera of this class of helminths. Fortunately practically all of the human trematodes utilize only gastropod molluscs and these are further limited primarily to fresh-water and amphibious species.

For study, the gastropods (snails), which are suspected on epidemiological evidence of harboring intermediate stages of human trematodes, are collected and taken or sent to the laboratory. Living non-operculate (*e. g.*, pulmonate) species cannot usually be shipped any great distance without considerable difficulty. They may be packed in damp (not wet) moss or clean cotton in a perforated container and if kept cool may survive for several days *en transit*. On the other hand, operculate snails, particularly the smaller forms, if they are first dried off and packed in dry moss in a perforated wooden box, will survive shipment for many days. Specimens of *Oncomelania* may be easily transported in this way for a month or more and will survive desiccation up to approximately six months.

In preparing the fleshy body of the snail for examination, the calcareous shell is carefully cracked by use of bone cutters and the inner portion of the spire "unscrewed" from the viscera. The organs most commonly parasitized are the "liver" (*i. e.*, digestive gland) and the hermaphroditic organ, which occupy the apical part of the snail. In ordinary practice these organs are separated from the remaining viscera and muscular portion and are teased apart in a watch-glass in half normal saline solution, which is approximately the saline concentration of the snail tissues. Trematode infections, if present, will usually be situated in the lymph spaces which bathe these organs. The dissected tissues are viewed under low power of the microscope. In moderate or heavy infections sporocysts or rediæ and cercariæ in various stages of development can easily be found. For careful study the individual specimens are transferred to a slide and mounted with a cover-glass. The best opportunity for observing details of the inner structure of sporocyst, redia or cercaria presents itself after the specimen has been somewhat compressed and usually just before the organism disintegrates.

III. Vertebrata.—*Fishes.*—Certain trematodes which parasitize man occur as encysted metacercariæ in the tissues of fishes. These cysts may be attached to the under side of the scales or to the cartilaginous tissues of the head and gills, or may be embedded in the subcutaneous or muscular tissues. The scales may be scraped off the fish's body for examination: cysts embedded in the flesh may be determined [illegible] of a "trichina" [illegible], sectioned, stained and then examined.

Pseudophyllidean cestodes which utilize fishes as intermediate hosts, are found in the sparganum or mature larval stage in these hosts. In infected specimens these larvæ will be found to occur as small, milky-white ribbons among the muscle ele[illegible] the flesh. However, there [illegible] ecies of *Diphyllo-*

Larvæ of *Dioctophyma renale* occur in adventitious capsules in the fish. Larvæ of *Gnathostoma* are found in similar situations.

Frogs, Snakes and Birds.—The only human helminths commonly occurring in these hosts are the spargana of *Diphyllobothrium* species. These occur as milky-white ribbons in between the muscular elements and are most commonly found along the spinal column, and in frogs in the thigh region and in snakes along the ribs. They also frequently reside in the subcutaneous tissue and in heavy infections give a puffy appearance to the animal. Likewise, larvæ of *Gnathostoma* have at times been recovered from snakes.

Mammals.—Sparganum infection is usually found in the same region in mammals as in lower vertebrates, but in the sparganum stage of *Diphyllobothrium* in the hedgehog, *Erinaceus dealbatus*, the pectoral muscles are most usually parasitized. Cysticerci are most commonly found in the heart muscles, hypoglossus and "tenderloin" regions, but may occur in all muscular tissues and to a lesser extent in other organs. *Multiceps multiceps* is most frequently encountered in the brain. *Echinococcus* cysts are most common in the vicinity of the liver, but may develop in any tissue of the body. *Trichinella* cysts are present in all striped muscle, but can be diagnosed most readily from a piece of diaphragm flattened in a "trichina" press, or, in lighter infections, by digestion in artificial gastric juice, then washed and concentrated by centrifugalization.

IV. Plant Vectors.—In all of the species of aquatic or semi-aquatic plants which serve as vectors of human helminths, including flukes of the species *Fasciola hepatica*, *F. gigantica*, *Fasciolopsis buski*, *Dicrocœlium dendriticum* and *Eurytrema pancreaticum* (?), and several species of strongylate nematodes, the mature larval worms are encysted as little spherules (trematode infections) or ensheathed larvæ (*Hæmonchus*

helminths, the species parasitic in man constitute a relatively small part of the total number of species harbored by these animals. This is particularly true of the stages of trematodes in molluscs and fishes and of nematodes in blood-sucking Diptera and beetles. For this reason the greatest care must be taken to determine that the larval helminths found in non-human hosts are actually the ones which infect man. To this end both morphological and experimental data are required in order that the evidence may be thoroughly convincing.

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Diplopoda.—For examination of species of *Julus* and *Fontaria* for *Hymenolepis diminuta* the technic is similar to that for *Coleoptera*.

II. Mollusca.—Molluscs are the first intermediate hosts of all digenetic flukes, and constitute an extremely important group to the student of trematode infections

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serve as vectors of human helminths, including flukes of the species *Fasciola hepatica*, *F. gigantica*, *Fasciolopsis buski*, *Dicrocœlium dendriticum* and *Eurytrema pancreaticum* (?), and several species of strongylate nematodes, the mature larval worms are encysted as little spherules (trematode infections) or ensheathed larvæ (*Hæmonchus contortus et al.*) on the outside of the vegetation, and never within the plant tissues. The fluke cysts appear as minute, milky-white concretions, attached to the surface of the plant. These larvæ may be discovered by carefully examining vegetation in endemic foci with a good high-power hand lens. They can be scraped off onto a slide, mounted and studied under a dissecting or compound microscope.

In all of the organisms which serve as intermediate or reservoir hosts of human helminths, the species parasitic in man constitute a relatively small part of the total number of species harbored by these animals. This is particularly true of the stages of trematodes in molluscs and fishes and of nematodes in blood-sucking Diptera and beetles. For this reason the greatest care must be taken to determine that the larval helminths found in non-human hosts are actually the ones which infect man. To this end both morphological and experimental data are required in order that the evidence may be thoroughly convincing.

CHAPTER XXXVI

ANTHELMINTICS AND THEIR USE

INTRODUCTION

Definition.—Anthelmintics are therapeutic agents used to destroy parasitic helminths residing in the host's body or to remove these parasites from the body If the anthelmintic kills the worms, it is referred to as a *vermicide*. if it produces evacuation of the worms without their death, it is only a *vermifuge*. Some helminths, as those residing in the blood vessels (*i. e.*, schistosomes), in the lymphatic vessels, lymph nodes or lymphatic tissues (*i. e.*, Bancroft's filaria), in the parenchyma of the lungs (*i. e.*, lung flukes), in the musculature (*i. e.*, *Trichinella* larvæ or cysticerci) offer a special therapeutic problem, even if specific chemotherapeutics are available, since the dead or dying worms or their eggs cannot be evacuated from the body, but must be absorbed as they disintegrate, else they may produce abscesses or provoke fibrocytic encapsulation.

An ideal anthelmintic is one which is lethal to the helminth well within the tolerance of the patient. In order to have an intelligent appreciation of the rational use of anthelmintics, it is first necessary to diagnose the specific infection, to visualize the position of the worms in the body, to know their approximate number, and to estimate the local and systemic effects of the worms on the patient. It is essential to know the therapeutic agent or procedure most useful in a particular helminthic infection or group of infections, but even more important is a knowledge of the dangers attendant on the administration of each anthelmintic, its contraindications and the most satisfactory procedures for safeguarding the patient before, during and following anthelmintic medication.

ANTHELMINTICS OF ANCIENT, MEDIÆVAL AND PRIMITIVE PEOPLES

The earliest extant record of an anthelmintic and its use is found in the Eber's papyrus (ca 1550 B C.) "Heltu," a common helminthiasis of Ancient Egypt, was treated with an infusion of the bark of the pomegranate tree (*Punica granatum*). Because of the more or less specific action of this plant product on tapeworms, and because of the extensive present-day distribution of the beef tapeworm (*Tænia saginata*) among Egyptians, Arabs and Ethiopians, it seems altogether likely that the priest-physicians of the Egyptian Middle Kingdom prescribed pomegranate bark for *Tænia saginata* infection. The Egyptians were also familiar with castor oil. [illegible] purgative, honey, which formed the medium for [illegible] many prescriptions. [illegible] d as vermifuges by the Abyssinians. *The Chaldean records thus far discovered do not refer to parasitic* worms or their treatment, and ancient Hindu records provide no positive information on the subject. Nor do the Hebrew texts contain references to intestinal parasites or their eradication.

The first known Greek reference to an anthelmintic is that of *Hippys Reginus* (ca. 490 B.C), who recommended the use of southernwood (*Artemisia abrotanum*)

for tapeworm infection in a woman. Democritus mentioned the use of mint for the evacuation of both roundworms and tapeworms. In his *Materia Medica*, Hippocrates, who had studied in Alexandria, described 300 plant products, 150 animal products and 36 minerals. The plant products which he regarded as having anthelmintic value include gum of acacia, anise seed, cardamom seed, cassia, colocynth, coriander seed, cumin seed, elderberry, fennel, garlic, hellebore, mulberry, myrrh, olive oil, pepper, pomegranate, rue, scammony seed, spearmint, turpentine, veratrum and walnut hull, all of which were repeatedly recommended as anthelmintics in later Greek, Roman and the early mediæval texts. Hartshorn and honey were among the animal products listed. Pomegranate, olive oil, hartshorn and honey are known to have been Egyptian contributions, pepper came, by way of India, from the spice islands off the Malay peninsula, and the other products were probably native to Grecian domain of Hippocrates' time.

Theophrastus of Eresus, physician, botanist and student of Aristotle, (ca. 300 B.C.) apparently first recommended fern root (πτέρις) as an anthelmintic. He stated that the sap of the *female* plant, when administered in sweet wine, was specific for evacuation of the tapeworm, and when drunk with barley water removed roundworms. Moreover, he described the difference between the fronds of the female and the male plant. Aurelius Cornelius Celsus, (*De re medicina*), who lived about the time of Tiberius Caesar, added the following as anthelmintics: bitter lupine, nettle, water cress and wormwood (*Artemisia absinthium*).

Most detailed in his consideration of anthelmintics was Dioscorides, a Greek army surgeon in the employ of Nero (ca. 60 A.D.). He was the first compiler of a comprehensive *Materia Medica*. He not only indicated the part of the plant or animal product to be utilized, but described the type of preparation and prescribed the amount to be administered. For example, he stated that 4 drachms of an aqueous emulsion of fern root, to which should be added an equal amount of scammony or black hellebore, was effective in banishing tapeworms. The evacuation was expedited, moreover, if the patient had previously consumed garlic. Prescriptions given by Dioscorides, and not previously mentioned, included calamint, coarsely ground up or heated in water, and drunk with salt or honey, to expel seatworms, and decoction of camomile with wine or marine absinth (*Artemisia maritima* or Oriental wormwood), bruised and chewed with raisins or figs, for ascariasis. Dioscorides also recommended drawing plasters, placed on the abdomen to assist in evacuating worms. Finally, he stated that axle grease, when placed within and around the anal sphincter, killed seatworms.

Pliny the Younger (*Historia naturalis*, 79 A.D.) was apparently more concerned with centipede and scorpion stings and with maggot infestation than he was with intestinal parasites. Nevertheless, he stressed the medical importance of tapeworms, reiterated the value of previously recommended anthelmintics, especially male-fern (first designated by him as *filix-mas*), and among other products added elecampane, beet root and iris to the pharmacopeia of his day.

Herodotus, the physician, (130 A.D.) was first to recommend the seed of santonica or Levant wormseed[1] (obtained from Turkestan), as well as the juice of *Plantago*, to expel worms. Galen (131-201 A.D.) referred to the common occurrence of seatworms in children and advised calamint juice as a remedy. The writings of Severus Scammonius (240 A.D.), Oribasius of Constantinople (360 A.D.), Aëtius of Antioch (540 A.D.), Alexander of Trolles (550 A.D.), Isidorus (570-636 A.D.), Paul of Ægina (ca. 670 A.D.) and Photius (891 A.D.) contributed no new information to the chemotherapy of parasite infections, although all of these workers discoursed at length on helminths and recommended many of the anthelmintics used by their predecessors.

[1] Because of its vermicidal action this product became known as "semen contra," meaning "semen contra vermes."

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An ideal anthelmintic is one which is lethal to the helminth well within the tolerance of the patient In order to have an intelligent appreciation of the rational use of anthelmintics, it is first necessary to diagnose the specific infection, to visualize the position of the worms in the body, to know their approximate number, and to estimate the local and systemic effects of the worms on the patient. It is essential to know the therapeutic agent or procedure most useful in a particular helminthic infection or group of infections, but even more important is a knowledge of the dangers attendant on the administration of each anthelmintic, its contraindications and the most satisfactory procedures for safeguarding the patient before, during and following anthelmintic medication.

ANTHELMINTICS OF ANCIENT, MEDIÆVAL AND PRIMITIVE PEOPLES

The earliest extant record of an anthelmintic and its use is found in the Eber's papyrus (ca 1550 B.C.) "Heltu," a common helminthiasis of Ancient Egypt, was treated with an infusion of the bark of the pomegranate tree (*Punica granatum*) Because of the more or less specific action of this plant product on tapeworms, and because of the extensive present-day distribution of the beef tapeworm (*Tænia saginata*) among Egyptians, Arabs and Ethiopians, it seems altogether likely that ... physicians of the Egyptian Middle Kingdom prescribed pomegranate ...

the Abyssinians The Chaldean records thus far discovered do not ... worms or their treatment, and ancient Hindu records provide no positive information on the subject Nor do the Hebrew texts contain references to intestinal parasites or their eradication.

The first known Greek reference to an anthelmintic is that of Hippys Reginus (ca. 490 B C), who recommended the use of southernwood (*Artemisia abrotanum*)

for tapeworm infection in a woman. Democritus mentioned the use of mint for the evacuation of both roundworms and tapeworms. In his *Materia Medica*, Hippocrates, who had studied in Alexandria, described 300 plant products, 150 animal products and 36 minerals. The plant products which he regarded as having anthelmintic value include gum of acacia, anise seed, cardamom seed, cassia, colocynth, coriander seed, cumin seed, elderberry, fennel, garlic, hellebore, mulberry, myrrh, olive oil, pepper, pomegranate, rue, scammony seed, spearmint, turpentine, veratrum and walnut hull, all of which were repeatedly recommended as anthelmintics in later Greek, Roman and the early mediæval texts. Hartshorn and honey were [illegible] hartshorn and honey are [illegible] way of India, from [illegible] lucts were probably native to Grecian domain of Hippocrates' time.

Theophrastus of Eresus, physician, botanist and student of Aristotle, (ca. 300 B.C.) apparently first recommended fern root (*πτερίς*) as an anthelmintic. He stated that the sap of the *female* plant, when administered in sweet wine, was specific for evacuation of the tapeworm, and when drunk with barley water removed roundworms. Moreover, he described the difference between the fronds of the female and the male plant. Aurelius Cornelius Celsus, (*De re medicina*), who lived about the time of Tiberius Caesar, added the following as anthelmintics: bitter lupine, nettle, water cress and wormwood (*Artemisia absinthium*).

Most detailed in his consideration of anthelmintics was Dioscorides, a Greek army surgeon in the employ of Nero (ca. 60 A.D.). He was the first compiler of a comprehensive *Materia Medica*. He not only indicated the part of the plant or animal product to be utilized, but described the type of preparation and prescribed the amount to be administered. For example, he stated that 4 drachms of an aqueous emulsion of fern root, to which should be added an equal amount of scammony or black hellebore, was effective in banishing tapeworms. The evacuation was expedited, moreover, if the patient had previously consumed garlic. Prescriptions given by Dioscorides, and not previously mentioned, included: calamint, coarsely ground up or heated in water, and drunk with salt or honey, to expel seatworms, and decoction of camomile with wine or marine absinth (*Artemisia maritima* or Oriental wormwood), bruised and chewed with raisins or figs, for ascariasis. Dioscorides also recommended drawing plasters, placed on the abdomen to assist in evacuating worms. Finally, he stated that axle grease, when placed within and around the anal sphincter, killed seatworms.

Pliny the Younger (*Historia naturalis*, 79 A.D.) was apparently more concerned with centipede and scorpion stings and with maggot infestation than he was with intestinal parasites. Nevertheless, he stressed the medical importance of tapeworms, reiterated the value of previously recommended anthelmintics, especially male-fern (first designated by him as *filix-mas*), and among other products added elecampane, beet root and iris to the pharmacopœia of his day.

Herodotus, the physician, (130 A.D.) was first to recommend the seed of santonica or Levant wormseed[1] (obtained from Turkestan), as well as the juice of *Plantago*, to expel worms. Galen (131–201 A.D.) referred to the common occurrence of seatworms in children and advised calamint juice as a remedy. The writings of Severus Scammonius (240 A.D.), Oribasius of Constantinople (360 A.D.), Aëtius of Antioch (540 A.D.), Alexander of Trolles (550 A.D.), Isidorus (570–636 A.D.), Paul of Ægina (ca. 670 A.D.) and Photius (891 A.D.) contributed no new information to the chemotherapy of parasite infections, although all of these workers discoursed at length on helminths and recommended many of the anthelmintics used by their predecessors.

[1] Because of its vermicidal action this product became known as "semen contra," meaning semen contra vermes."

MEDIÆVAL ANTHELMINTICS

was a shining star.
th the early Greek physicians that worms arose from fermentation and putrefaction of foodstuffs taken into the body, particularly raw meats and uncooked vegetables and fruits. Hence, he argued, a proper diet would do much to reduce their numbers. He recognized four types of helminths, namely, (1) long worms, (2) flatworms, (3) small worms and (4) round worms. Most authorities interpret these respectively as (1) the beef tapeworm, *Tænia saginata,* (2) individual detached proglottids (*i. e.,* "segments") of the beef tapeworm, erroneously regarded by Avicenna and later workers as complete worms, (3) the seatworm, *Enterobius vermicularis,* and (4) the large roundworm, *Ascaris lumbricoides.* On the other hand, Khalil (1922) considers the first to be ascarids, the second tapeworms, the third seatworms and the fourth hookworms. In the present writer's opinion, the intrinsic evidence presented by Avicenna himself, both as published in Venice, 1562, *fide* Davaine (1860) and in Khalil's own English translation from the 1131 A.D. manuscript copy of the original text in the British Museum, favors the former interpretation as the more plausible one.

Avicenna recorded pyrexia, intense hunger, and at times acute ileus and epilepsy as occasioned by intestinal worms, which might even perforate the bowel. He stated that the "round worms" were more common in the young, the "long worms" in older people Both the "flat worms" and the "small worms" migrated out of the anus.

Avicenna listed many medicaments to be used in expelling these worms. More-

extract of pomegranate bark and male fern root; among the adjuvants, garlic,
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duce
systemic toxemia. He also stated that a febrile condition contraindicated anthelmintic treatment. For two days preceding specific therapeusis he advised a diet restricted to milk For seatworms he prescribed high saline enemata

Granting that Avicenna discovered no new anthelmintics and recommended none not already known to the ancient Greeks, he was the first physician to relate the worms to the symptoms they produced and the first to institute rational treatment for the infections. A mediæval sufferer from intestinal helminthiasis could have had full confidence in Avicenna as his physician.

Greek belief was tenaciously espoused, that worms were engendered by putrefaction within the "stomach" (an instance of effect mistaken for the cause), supernatural
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moon and its rejuvenati
influenced by the moon, but I speak from my constant experience, which recognizes the cause of these events A number of children have presented worms to me with such regularity, that without the almanac, I know from the return of these children

the day of the month, and this has obliged me to believe." In consequence, he, along with many other physicians from the time of Nicolas Myrepsus, a Greek physician of the 13th century, prescribed anthelmintic medication towards the end of the lunar month. Other physicians as late as 1855 similarly prescribed treatment for *Ascaris* and seatworms according to the phase of the moon.

Gradually the more important anthelmintic prescriptions of the Greeks and Romans, as well as the teachings of Avicenna, were forgotten, and consequently it may be assumed that the burden of helminthic infections of mankind correspondingly increased. Practically every writer on philosophy, natural history or physic of this period mentioned the prevalence of worms, which now became possessed of spirits, with eyes, ears, nostrils, horns, feet and, at times, with many heads. Each and every scribe recommended a plethora of alleged new specifics against worms. Little by little the most common prescription advocated was a powder of dry worms ("semen lumbricorum"), which had been previously passed by a patient, based on the seemingly irrefutable argument, "similia similibus curantur."

Towards the end of the sixteenth century there was evidence of a rediscovery of the works of the ancient physicians and of Avicenna. The most interesting document which the present author has had an opportunity to examine is not cited in helminthological literature. It is a beautifully tooled, parchment-bound volume, entitled "Artzneybuch," by Osswaldt Gaebelthauern, court physician to the prince of Wuertemberg (Tuebingen, 1599). In part one (pp. 260–268) there is a short section entitled "fuer die Wuerm." In this brief compendium on anthelmintics forty separate prescriptions were recommended. Several of these, which indicate the state of anthelmintic practice in South Germany at the end of the 16th century, have been copied in free translation

1. *For worms, especially in children:* (administer) in warm milk on three successive mornings, one-eighth ounce of hartshorn, obtained on the thirtieth of the month; subsequently, (take) no food for three hours.

2 Take a worm which has been passed by a person, burn it to powder, and administer it in food or drink.

3 Mix Venetian (Levant?) wormseed and honey over a fire. Take one spoonful mornings and evenings on an empty stomach.

4 Drink cold olive oil This drives out the worms.

5 *When a person is annoyed with worms leaving the body by the anus or the mouth* ("hinden oder vornen") take three handfuls of licorice (root), one handful of fern root and one handful of fennel leaves Steep in three parts of water until only three fingers (height) of the decoction remains. Inhale the vapor.

6 Take pulverized quince leaves and administer with milk. The worms then die An infusion of the leaves, placed (as a poultice) on the navel, drives out the worms In summer utilize the sap of this plant

7 *For worms in someone else's belly* steep pimpernel in vinegar Drink for seven days and the worms will come out of you dead

8 Steep garlic in vinegar and drink some every day.

9 *Powder for worms* Rec Seminis Cinæ (i e, Levant wormseed), drach i. s; cornu cervi viti, drach. i; seminis Portulacæ, Caulium, an. scrup i.; Spodii de Canna, scrup s, Rhubarbi, drach. s; Sacchari, drach i s. Fiat omnium Pulvis; misce

10 *For worms gnawing in the belly:* take large fern roots, dug in May or on the 30th of the month Cut to shreds and pulverize Give to young and old It certainly drives out the worms

11 *For driving out nests of worms:* take garlic, honey and mustard seed Mix well Administer on an empty stomach for three mornings and nights as a "spread" (i e, like butter on bread). In this way it (i. e, the worm) leaves him

12 Take a sufficiently large piece of "spotted root" ("Scheckwurz"). Make a

hole in it and fill with honey.
rectum and again withdraw it.
on it like small lice. One must
flesh or of lean bacon. Bind in long conical strips with stout twine or string. Insert into the rectum and the little worms will come out, as has been frequently demonstrated

13. *For* ... he patient drink notl ... at goat's milk in a ... that the vapor from the milk may ascend to him. In this way the worm is drawn out as desired. Afterwards have him eat pimpernel.

From these prescriptions there is intrinsic evidence that several of the ancient prescriptions, as hartshorn, Levant wormseed, fern root, garlic, etc. were known to the author, and abstinence from food before taking these drugs suggests a knowledge of Avicenna's teachings. However, the inhalation of the vapor of the anthelmintic decoction (*vide* No. 5), and the use of navel poultices (*vide* No. 6) suggest that the distinguished court physician was not as logical in the administration of his specifics as was Avicenna. Moreover, fern roots dug in May might contain more anthelmintic virtues than those dug in December, but the advice to dig them on the 30th of the month (*vide* No 10) is obviously based on the superstition that the moon exerted an influence on the crude drug as well as on the worm. The ingenious methods recommended in prescriptions Nos. 12 and 13 are apparently discoveries of Gaebelthauern's own times, but have survived as grandmother's remedies until the present day.

Unquestionably the author of the Artzneybuch was dealing with *Ascaris* (*vide* Nos. 3, 8), seatworms (*vide* Nos. 11, 12) and tapeworms (*vide* Nos. 5, 10, 13), although *in no instance does he directly describe these worms*

The 17th century was particularly notable for the extension to the field of anthelmintic therapy of mercury, which had been used for some years in the treatment of syphilis It was prescribed in the metallic form, as a decoction, as an infusion distilled with wine, or as cinnabar. Other heavy metals and their salts were also commonly administered as anthelmintics during this period, including gold, copper, iron, tin, et ... were soon found to be particularly ... hence caused lead poisoning ... til the middle of the 19th century. The English product was believed to be the least dangerous.

If Godofredus Sikardus, who published "De Anthelminticis" in 1698 (University ... there was no important ... century. ... was Madame Nouffer's celebrated tapeworm remedy. For twenty years a secret, this prescription was utilized by *Morat in Switzerland and then by* Madame Nouffer after her husband's death, to treat patients who came from all over Europe to be divorced from their tapeworms ... was ... reat- twice cured a ... f the ment. Finally ... gate success of the remedy (1772) appointed a commission of physicians to ... report, its alle ... ab- whereu ... ian lished ... urs

teenth

and nineteenth centuries the materia medica of Europe was gradually increased and enriched by the introduction of many plant products from the Americas, the East Indies, and from Abyssinia. Among these were several valuable anthelmintics.

From the Americas there were obtained such household remedies of the pre- [illegible] East Indies and of Tropical America, (iii) *Ficus glabrata* and related species, the sap (*i. e., leche de higuerón*) of which was used by the natives of Central America and Northern South America to eradicate intestinal helminths; (iv) *Fucus helminthocorton*, a sea-weed originally found on the coast of Argentina, but so popular with the inhabitants of Corsica, after its introduction into Europe, that it became known as "Corsican moss;" (v) *Mucuna pruriens*, or cowhage, a legume of Tropical America, whose spinose pods caused a profuse diarrhea when consumed; (vi) *Schoenocaulon* (syn. *Veratrum*) *officinale*, the cevadilla of Mexico, which was commonly confused with the European hellebores, and (vii) *Spigelia marilandica*, the pinkroot of the United States, together with its Tropical American relative, *Spigelia anthelmia* (Indian pink) which had been used for many centuries in Brazil as a vermifuge.

From India and Malaya there came *Areca catechu*, the betel or areca nut, commonly utilized in ancient times by the Chinese and mentioned as an anthelmintic by Avicenna but forgotten for centuries; from the Moluccas and Reunion, *Carica papaya*, or papaya, containing the active principle papain; from the East Indies, the coconut; from the East Indies and the Philippines, *Mallotus philippinensis* or kamala, and from Central and Southern Asia, *Melia azadrichta* or azedarach.

Likewise, explorers in Abyssinia discovered two important native trees, whose products were considered by the natives to have specific anthelmintic value, namely *Acacia anthelmintica* or musenna and *Hagenia abyssinica* (syn. *Brayera anthelmentica*), the kousso.

Probably the most valuable commentary on anthelmintics utilized in Europe and the United States at the close of the eighteenth century was the "Lezioni medico practiche sopra i principali vermi del corpo umano vivente e le così dette malattie verminose," published in 1802 by Dr. Valeriano Luigi Brera (1802), professor extraordinary of practical medicine in the University of Pavia (later translated into German, French and English). The English translation (1817), which the present author has studied, bears evidence of both a logical and a practical grasp of the subject. In notes to his Fourth Lecture, Brera states (p. 353): "if any one, not having a medical education, should think of prescribing anthelmintic medicines, he is desired to reflect, that this cannot be done either with safety or any prospect of advantage, till he shall acquire the following information: a knowledge (i) of the structure of the human body, (ii) of the vital properties and functions of the various organs of this complex system, in a sound state; (iii) of the deviations from this state, which occur in the many diseases of which the body is subject, and (iv) of the medicinal virtues of the several articles called anthelmintic, both as they affect the intestinal worms, and the living body they inhabit." This advice is as comprehensively sane today as it was in 1802.

Brera's treatise was the first critical, really scientific presentation of the subject since that of Avicenna, but had the distinct advantage of profiting from the physiological and clinical discoveries of the 17th and 18th centuries.

Of the multitude of plant products prescribed as anthelmintics during this period, only the following were mentioned by Brera: *Allium cepa* (onion), *Allium sativum* (garlic), *Artemisia maritima* (santonica), *Chenopodium ambrosioides* var. *anthelminticum* (American wormseed), *Convolvulus jalappa* (jalap), *Angelica archangelica*,

16 cases treated, of which 1 was a known failure because the patient vomited the drug, four had no adequate follow-ups and the remainder either passed the head along with the major portion of the worms, or were found to be worm-free ten or more months after treatment.

Sandground's regimen of therapy was to prescribe 3 to 4 cc. of carbon tetrachloride in a little water or milk. "It is not at all necessary that the *patient be starved before treatment or that there be a preliminary* purgation, but on general principles patients have been advised to restrict their supper to toast and milk, and to have an enema on the evening before taking the treatment. The drug is given the first thing in the morning, the patient refraining from eating until good purgation has occurred. The tapeworm is usually expelled within two or three hours after treatment and thereafter the patient may resume normal activity." This investigator (loc. cit.) states that the drug has always been well tolerated, although some dizziness and drowsiness were experienced during the first hour following administration of the drug In the present author's limited experience with this anthelmintic in tæniasis, with Glauber salts purgation the night before treatment and with the patient comfortably settled in bed at least one-half hour before administration, the patients suffered severe colicky pains in the stomach shortly after taking the prescription and were extremely uncomfortable until adequate bowel movements were obtained following post-treatment purgation. Within another hour the patients became comfortable, although they were weak and dizzy for several hours Sandground (loc. cit.) found carbon tetrachloride efficacious for beef tapeworm (*Tænia saginata*), pork tapeworm (*T. solium*) and fish tapeworm (*Diphyllobothrium latum*).

Tetrachlorethylene.—This drug, which is a chlorinated aliphatic hydrocarbon ($CCl_2 \cdot CCl_2$), possesses high efficiency in evacuating hookworms, combined with a very low degree of toxicity, due to the fact that it is only very slightly soluble in water and hence, in the absence of alcohol and absorbable fats, is practically all evacuated in the feces. Rogers (1944) ... and ... tic ... .9), ... 89.8 per cent, while Pessô... cent evacuation of Necat... nearly as high as that of ... and produce... kidneys ... e been ... post-transient headache and vertigo, which disappear rapidly ... post-treatment purgation. Kendrick (1929), Wright, Bozicevich and Gordon (1937), Hare and Dutta (1939) and Sandground (1941) have indicated that tetrachlorethylene occasionally produces grave manifestations of intoxication. Chaudhuri and Mukerj ... the first ...

... *acute hemorrhagic nephritis* as ... cause of death. Old stock of tetrachlorethylene or that which has been

subjected to considerable heat is likely to be useless. This condition may be discovered if, on opening a globule or stock bottle, phosgene gas is detected.

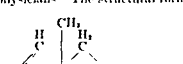
In order to give the drug ample opportunity to attack the hookworms, Glauber salts purgation (15 Gm. or ½ ounce in a glass of water) should be carried out the night before treatment, the drug should be administered in one dose on an empty stomach in the morning and should be followed in two hours by Glauber salts. Pessôa and Pascale (loc. cit.) obtained best results when the drug was taken in gelatin capsules. The standard therapeutic dose for an adult is 3 cc.; for children, 3 minims per year of age. Children may take it on a teaspoon with sugar.

In mixed infections of hookworms and *Ascaris* the drug may be mixed with oil of chenopodium in the amounts of 2.3 cc. of the former and 0.7 cc. of the latter, although a much safer and equally satisfactory proportion is 2.7 to 0.3 cc.

II. Terpenes

These are unsaturated hydrocarbons of the molecular formula $C_{10}H_{16}$. Many of them occur in nature as essential vegetable oils. Important members of the group are terpene, camphene and limonene. Two of the terpenes, *santonica* and *oil of chenopodium*, have played an important rôle in anthelmintic medication since ancient times.

Santonin.—This is the neutral principle extracted from Levant wormseed (*Artemisia cina*) and other related species of *Artemisia* which were used in an unrefined form by the early Greek physicians. The structural formula is



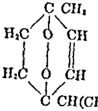
It is odorless, colorless, but becomes yellow on exposure to light. It is almost insoluble in cold water but dissolves moderately well in alcohol and chloroform.

Santonin does not irritate the mucus membranes, is readily absorbed from the bowel wall and is practically non-toxic to the respiratory and circulatory systems. However, it is especially harmful to the central nervous system and the centers of the special senses, which it tends to paralyze (Desoille, 1937). Elimination is mostly via the kidneys.

As an anthelmintic for *Ascaris* its effect is rarely, if ever, vermicidal. A tolerated dose (0.06 to 0.2 Gm.) is effective only when combined with calomel (0.2 to 0.3 Gm.) and followed within 3 hours by saline purgation. Hall and Augustine (1929) assign an *Ascaris* removal rate of 27 per cent to santonin. Although pyrexia is not a contraindication, it should never be administered on an empty stomach or with absorbable oils. Following its administration there are usually some ill-effects, varying in type and degree, including mild or severe diarrhea or enteritis, headache, vertigo, mental confusion, ocular disturbances, hallucinations, convulsions, extreme weak-

ness, prostration, drowsiness and, on rare occasions, coma. (Desoile, 1937). The literature contains reports of cases with slow and feeble pulse, syncope due to rapidly lowered blood pressure, albuminuria or hematuria and painful micturition, attributed to santonin therapy.

Oil of Chenopodium.—*Oil of chenopodium* or oil of American wormseed is obtained from "the overground parts of the flowering and fruiting plant of *Chenopodium ambrosioides* var. *anthelminticum*." It contains as its effective principle 60 to 80 per cent ascaridol, which has the following structural formula:



It is a liquid organic peroxide which is colorless, volatile, unstable and has a very pungent odor. The crude product was used by the Cherokee and Mayan Indians nearly two hundred years ago.

This potent anthelmintic is extremely irritating to the skin and mucous membranes, it produces slow, weak pulse and depresses the circulation. The therapeutic dose is 1.5 to 3 cc., most satisfactorily given in three divided doses one-half hour apart. Although it is probably more efficient without pre-treatment purgation, saline catharsis the night before treatment provides a partial safeguard against its toxic effects. One or two hours after treatment saline purgation is essential, since the drug inhibits peristalsis. It is readily absorbed from the intestinal wall and is excreted over a long period of time by both the lungs and the kidneys. The full therapeutic dose (3 cc. for an adult, 3 minims for each year of age in the case of children) is near the minimum lethal dose, and usually provokes marked gastro-intestinal disturbance, heachache, and, too frequently, complete prostration, profound systemic toxemia and death. Desoile (1937) has reported that a first dose sensitizes the intestinal wall so that subsequent doses are absorbed more readily. In addition to ataxia the following disturbances of the sensorium have been observed: tinnitus, vertigo, deafness up to two years, visual hallucinations, marked reduction in vision, and blindness. These latter unfortunate sequelæ usually do not appear until several days or even a few weeks after administration of the drug. It is contraindicated in nephritis, organic heart disease, intestinal ulceration or hepatitis. It should never be prescribed except under the immediate supervision of a physician.

Although oil of chenopodium, or its refined principle ascaridol, is a very efficient ascaricide (83.2 per cent worm reduction rate with 1.5 cc. of the drug, 94.9 per cent with 2 cc. administered, according to Caldwell and Caldwell, (1929), its use is today probably not warranted except in greatly reduced amounts in combination with carbon tetrachloride or tetrachlorethylene, for patients harboring both hookworms and *Ascaris*. Thus, 2.7 cc. of carbon tetrachloride or (preferably) tetrachlorethylene and 0.3 cc. of oil of chenopodium may be prescribed for an adult, with the expectation of considerable margin of safety combined with effective results.

This combined therapeusis, given in one dose, should invariably be preceded the night before by saline purgation (15 Gm. or one-half ounce of Glauber salts in a glass of water), should be given on a fasting stomach and should be followed in one or two hours by a saline purge. For children the combined dose should not exceed three minims per year of age, and may be administered on a teaspoon with sugar.

[illegible]

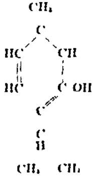
highly toxic properties in therapeutic amounts (1.5 to 3 cc.), oil of chenopodium is no longer used alone in hookworm disease or trichocephaliasis.

In past years this preparation has been used with demonstrated efficiency in the treatment of dwarf tapeworm infection (Stitt, 1929). Since this infection is most common in small children and the dangers resulting from administering this drug are potentially very grave, it should not be employed. Patients should be warned against taking proprietary vermifuges which at times contain ascaridol.

III. Phenols

These are hydroxy-compounds which are derived from the aromatic hydrocarbons by the substitution of hydroxyl-groups for atoms of hydrogen and become united directly with carbon of the nucleus. They are conveniently subdivided into (a) monohydric, (b) dihydric and (c) polyhydric series. Anthelmintics of the first series include *thymol* and *beta-naphthol*, those of the second series, *crystoids anthelmintic*, and those of the third series, *filicic acid* (the effective principle in *Aspidium filix-mas*)' and *kamalin* (in *kamala*).

Thymol.—This drug, which is obtained from several species of plants and is supplied in pure crystalline form, is methyl-isopropylphenol ($C_{10}H_{14}O$), a monohydric phenol. Its structural formula is

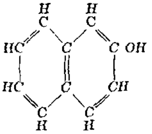


It consists of colorless, translucent crystals, which have a characteristic pungent odor, is sparcely soluble in water, highly soluble in alcohol, chloroform, ether and olive oil. It has been used for the eradication of hookworm since 1879, and soon thereafter became generally adopted for this use, although the first critical pharmacological and clinical tests were carried out by Caius and Mhaskar (1919). These investigators stated that thymol is a powerful vermicide and that any amount of the drug from 30 to 60 grains (2 to 4 grams), administered in one dose, will prove

effective in elminating hookworms. They claimed that it had essentially no toxic effects on the patient and was eliminated from the system within twenty-four hours Futhermore, they found purgation before or after treatment was not essential for satisfactory results Darling (1920) obtained an average of 88 6 *per cent worm removal* after a single dose of 60 grains (4 Gm), administered one hour after Epsom salts purgation, while Ashford and Igaravidez (1911) obtained 68 8 *per cent cures* after several courses of treatment extending over thirty days. Chopra (1936) recommends for an adult two or three divided doses of from one to two Gm. each (15 to 30 grains), powdered or finely granular, mixed with lactose or sodium bicarbonate and followed within two hours by saline purgation.

In spite of the claims of Caius and Mhaskar (loc. cit.) thymol has been found to have noteworthy toxic properties. It irritates mucous membranes At first it mildly stimulates, later it depresses the central nervous system It produces headache, tinnitus, extreme vertigo, a subnormal temperature, and collapse, if administered in excess. The kidneys are irritated by the drug and albuminuria is not uncommon following its administration.

Beta-Naphthol—This drug, which is a synthetic, white crystalline preparation, is β-hydroxynaphthalene, $C_{10}H_8O$, a monohydric phenol. Its structural formula is:

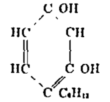


It is a whitish to yellowish-white crystal substance which darkens with age and on exposure to light, has a slight phenolic odor, dissolves sparcely in cold water but readily in alcohol, ether, glycerin and olive oil. It has been used to eradicate hookworms since 1904. Caius and Mhaskar (1921) first critically tested the efficiency of this anthelmintic and reported a 93 to 97 per cent hookworm removal rate with 3.3 grams (50 grains) given in 1 to 3 doses. They stated that it requires no post-treatment purgation and is safer to give than thymol.

In spite of the above claims, experience has shown it to be less efficient than thymol and much less efficient than either carbon tetrachloride or tetrachlorethylene for the removal of hookworms. Moreover, its toxic properties must not be passed over lightly, since it irritates mucous membranes, and in full therapeutic doses at times produces epigastric and abdominal pain, nausea, vomiting, diarrhea, muscle spasm, and depressed respiration, while its continued administration may result in hemolysis, convulsions, respiratory ... Micturition was frequently painful, urine ... in 83.3 per cent of Ashford's patients in Puerto Rico (Ashford and Igaravidez, 1911) Today β-naphthol is rarely used as an anthelmintic except in fasciolopsiasis. (*Vide* p 188.)

Crystoids Anthelmintic (Hexylresorcinol Crystoids).—This dihydric phenol is a white to light brownish crystalline substance.

Its structural formula is:



It has a pungent odor and a sharp, astringent taste It is practically insoluble in water (1:2000) but is readily soluble in alcohol, ether, chloroform and olive oil. Robbins (1931) demonstrated that about 70 per cent of the ingested dose is excreted unchanged in the feces and that the remainder is recovered from the urine as the ethereal ester Although the crystals of hexylresorcinol, on direct contact with the tongue and mucous lining of the mouth, produce a painless, very superficial erosion, single large doses or repeated doses over long periods of time fail to produce any

t

complaints of gastric distress when food is taken within two or three hours after its administration, hexylresorcinol may be stated to produce no ill-effects It has no essential contraindications if the recommendations concerning the methods of treatment are carefully followed

Today this drug is the safest and most efficient ascaricide. The crystoids, in hard gelatin capsules, are available in 0.1 gram and 0 2 gram amounts When taken in therapeutic amounts in a single dose on an empty stomach, with food omitted for 4 or 5 hours, so that the drug will not be absorbed by the food and thus be less efficient against the worms, hexylresorcinol has a worm removal rate of 84 to 92 per cent (Lamson, Brown, Robbins and Ward, 1931) and a cure rate at times as high as 75 or 80 per cent For an adult or a child over 10 years of age, 1 Gm is the therapeutic dose, for children of preschool age, 0.4 to 0 6 Gm , and for children in elementary schools, 0.6 to 1 0 Gm. Although it is not necessary to give post-treatment purgation to protect the patient from the toxic effects of the drug, it is desirable to provide purgation to evacuate dead and dying worms, whose by-products are very irritating to most patients

In a series of 530 cases of *Necator americanus* infection Lamson, Brown, Robbins and Ward (1932) obtained 80 to 89 per cent evacuation of the worms and 42 per cent cures with a single dose of one Gm of the drug, 85 to 97 per cent worm removal and 60 to 88 per cent cure with two consecutive daily doses of 0 6 Gm each These patients, mostly school children, were given saline purgation the night before treatment, refrained from taking their morning meal, fasted for 4 or 5 hours after treatment and were given post-treatment purgation, either with salts or mineral oil In the author's experience with uncomplicated hookworm infection crystoids anthelmintic in 1 Gm. amounts in one dose removes approximately 75 per cent of the worms.

The special advantage of this drug is its comparative efficiency and great safety in combined infections of hookworm and *Ascaris* The latter will

frequently all be removed with one course of treatment. If, in addition, there are about 500 hookworms present, approximately 375 will be evacuated with the first treatment, while a second course within a week will remove enough of the remainder to reduce the infection below the threshold of clinical importance.

Rogers (1944) found that the efficiency of crystoids anthelmintic might be increased by a technic to increase its activity through mucus and the cuticula of nematodes. He suggested the following: Reduce the mucous surface of the bowel wall with atropine; decrease the viscosity of the mucus; withhold food, and employ sodium oleate (0.2 per cent solution), sodium laureate (0.125 per cent solution) or an actual detergent to render the surface of the worms more permeable.

Crystoids anthelmintic has been demonstrated to be moderately lethal to the pinworm, provided the drug actually comes in contact with the worm (Faust, Dwyer and Casparis, 1937). Some of these worms in any given infection are usually present in the cecum and appendix, while others (usually gravid females) are migrating down the colon and rectum. Oral administration alone of this drug is usually effective only against the pinworms in the vicinity of the cecum. Hence the need for supplementary intra-rectal therapy in the form of high retention enemas of a 1:1000 solution of the drug.

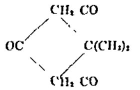
If the crystoids are administered as recommended, no discomfort is occasioned, but at times considerable colicky pain is produced by the retention enema, especially in small children, who may even develop signs of convulsions. In such an event the enema must be evacuated at once and a sedative (sodium amytal or sodium bromide) administered.

Using the usual therapeutic dose of crystoids anthelmintic (one Gm. for adults in hard gelatin capsules), Maplestone and Mukerji (1932) had no [illegible] *saginata*, in which follow-ups for [illegible] (1938) reported on 24 cases with [illegible] catharsis the night before therapeusis, this investigator gave the drug (1 to 3 Gm. in a single dose or up to 3 Gm. on each of two consecutive days) in a large amount of water. Mineral oil or saline purgation was given one hour after administration and food was proscribed for several hours. There were 7 apparent cures. Sandground (loc. cit.) commented that 1 gram may be effective in one patient and in another 3 grams may not be successful in removing the heads.

In children with dwarf tapeworm infection crystoids anthelmintic is the drug [illegible] a The a [illegible] child [illegible] Purgation the night before with Glauber salts (15 Gm. or ½ ounce in a glass of water), administration of the drug on an empty stomach about seven in the morning, and Glauber salts purgation about 9 A.M. are recommended as a rational procedure. The patient may take the usual noon meal if adequate bowel evacuation has been obtained. This treatment may be repeated again and again without danger to the patient. In case there is considerable diarrhea, better results may be obtained by omitting pre- and post-treatment purgation.

In 1937 McCoy and Chu used crystoids anthelmintic in the treatment of 129 cases of *Fasciolopsis buski* infection in China. For children 1 to 7 years of age 0.4 Gm. was administered; for older children up to 13 years of age, 1 Gm. Fifty-four per cent of the patients were cured and an additional 23 per cent had a 90 to 99 per cent reduction in their *Fasciolopsis* egg-count.

Aspidium filix-mas (Male fern).—This polyhydric phenol is the best known and most commonly used anthelmintic for all species of tapeworms, and is probably the drug of choice with most patients. It dates from early Greek medicine. It is obtained from the rhizomes and stipes of *Dryopteris filix-mas* (syn. *Aspidium filix-mas*) and at times from other closely related ferns. The British Pharmacopœia recognizes the extract, the U. S. Pharmacopœia, the oleoresin. The latter is possibly more potent but it is stated to be somewhat more toxic. The anthelmintic principle is *filicic acid* or *filicin*, an amorphous powder, which constitutes 24 per cent of the fresh oleoresin. Its structural formula is:



It is a white crystalline substance which is insoluble in water and sparingly soluble in alcohol and ether.

In preparation for treatment with the oleoresin of male fern the patient should be advised to abstain from eating any absorbable fats for forty-eight hours preceding specific medication and should preferably take only a semi-liquid diet the day before treatment On that night Glauber salts purgation (15 Gm or ½ ounce in a glass of water) is recommended. On the morning of treatment the patient abstains from food and is made comfortable in bed. At 7, 7:30 and 8 o'clock each an adult patient takes 0.6 to 1.2 cc. of the drug in capsules, while children take one minim for each year of age up to fifteen years. Two hours after the drug has been taken Glauber salts purgation is recommended. No food is permitted until there have been one or more copious bowel movements.

The quieter the patient remains during the treatment, the less likely are toxic symptoms to develop. Nevertheless, therapeutic doses may produce headache, vertigo, nausea, vomiting, severe abdominal cramps and diarrhea, less frequently bilirubinemia, jaundice, albuminuria, and dyspnea. On rare occasions, usually when instructions have not been carried out, there may be convulsions, loss of reflexes, optic neuritis or blindness, respiratory and cardiac failure These symptoms are due to the irritating properties of the drug on the gastrointestinal mucosa, possible necrosis of the liver parenchyma, paralysis of non-striated muscles, and excessive stimulation of the spinal cord

For children or adults the drug has been intubated in a single dose into the duodenum. In 1935 Golob introduced intra-duodenal intubation of an emulsion containing the oleoresin of male fern, mucilage of acacia and Epsom salts. This has been modified by the author and his associates by

replacing the Epsom salts with Glauber salts and reducing the amount of the anthelmintic to one-half that advocated by Golob, as follows (adult dosage): oleoresina aspidii, 4 cc.; muc. acaciæ, 30 cc., and sodium sulfate (saturated solution), 30 cc. The patient is prepared by Glauber salts purgation the night before treatment and on the morning of treatment takes no food. In the physician's office or clinic treatment room a duodenal sound is carefully passed, then the emulsion is slowly intubated. The patient remains in a resting horizontal position for about a half-hour before the tube is withdrawn. No post-treatment purgation is required. This method of administration has considerable advantage over the fractionated oral treatment.

Oleoresin of male fern should not be administered to patients who are profoundly anemic, to those who are debilitated, to the aged, to infants under one year of age and to pregnant women. However, if a pregnant woman is infected with *Tænia solium*, in order to obviate the potential grave danger of cysticercosis cellulosæ resulting from internal autoinfection, it may be necessary to risk treatment.

Desoile (1937) has called attention to ocular and other neuroses which may develop from systemic absorption of the effective principle of male fern. Clinically these include unilateral or bilateral blindness, severe amblyopia, cephalalgia, vertigo, drowsiness and even coma, tetanic seizures, trismus and intense opisthotonus. He states that hemolytic jaundice has also been observed as a sequela.

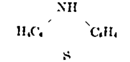
In the average case of tæniasis, if the oleoresin of male fern is administered according to recommendations, the scolex of the worm should be obtained in about 90 per cent of the cases. With intubation the cure rate is probably somewhat higher.

Kamala.—Since the days of the distinguished physician Davaine (1860) the French have favored kamala for broad fish tapeworm infection (diphyllobothriasis). The effective principle, *kamalin*, is a polyhydric phenol. The unpurified kamala is obtained from the glands and hairs covering the fruits of the East Indian spoonwood tree, *Mallotus philippinensis*. Neveu-[illegible]
Lemaire (1936) states that 6 to 12 [illegible]
to an adult, 0.5 to 1.0 Gm. (8.3 to [illegible]
fluid extract is used, the dose being [illegible]
to age. In case the worm has not been expelled within two hours after treatment, castor oil is administered.

IV. Phenylamines

The first member of this group to be isolated was analine oil, which was distilled from indigo in 1826. Diphenylamine is an intermediate product utilized in the dye industry. One member of this series, *phenothiazine* (thiodiphenylamine) was first tested as an insecticide, then as an anthelmintic in veterinary medicine and somewhat later for treatment of human enterobiasis.

Phenothiazine.—This is a light yellow, sublimable crystal powder prepared by fusing diphenylamine with sulfur in the presence of iodine. It is insoluble in water and sparingly soluble in organic solvents and mineral oil. Its structural formula is:

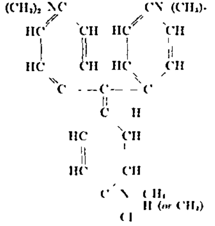


As an anthelmintic phenothiazine has been administered clinically by a number of persons, including De Eds *et al.*, Hubbe, Johnstone, Most, Sisk, Bercovitz, Manson-Bahr, Kuitunen-Ekbaum (1946), and Deschiens and Lamy (1947). In maximum tolerated doses the drug has an apparent 80 per cent eradication rate for *Enterobius vermicularis* following one course of treatment. Rather frequently in higher doses it has been accompanied by acute hepatitis, hemolytic anemia, albuminuria and hematuria. In tolerated doses (7 Gm. in 4 days for adults) it occasionally causes fever, rash, pruritus, edema, nausea and vomiting. Deschiens and Lamy (*l. c.*) advise that phenothiazine be withheld from children and be reserved for certain adults free of anemia, hepatitis and nephritis.

V. Methylrosanilines

This group is derived from triphenylmethane and constitutes an extremely important series of dyes. The product used medicinally is gentian violet, a dark green crystalline powder which dissolves as a 2.5 to 4 per cent solution in water, 10 per cent in alcohol and about 6.7 per cent in glycerin.

Gentian Violet (Medicinal).—Gentian violet medicinal is either pentamethyl or hexamethyl pararosanilin or a mixture of the two substances. Its structural formula is as follows:



Originally recommended as a specific for the Chinese liver fluke, *Clonorchis sinensis*, by Faust and Yao (1926), it was first tested and recommended in strongyloidiasis by DeLangen (1929) and was first used for this purpose in the Western Hemisphere by Faust (1930). DeLangen (loc. cit.) did not claim that gentian violet cured strongyloidiasis but stated that it usually alleviated symptoms and reduced the eosinophilia. During the past decade it has become the drug of choice in strongyloidiasis. The *standard course of treatment* for an adult consists in the oral administration of gentian violet med. U.S.P. in 1½-hr. Seal-Ins enteric coated tablets, designed to

discharge the maximum amount of the drug in the duodenum, where the worms are most concentrated in the mucosa. It is given before meals in the amount of two ½ grain (0.03 Gm.) tablets, t.i.d. until 50 grains (3.3 Gm.) have been taken.

Many of these cases have been freed of the worms by a single course of treatment, but some have remained infected even after two or more complete courses.

If cure is not effected by oral administration of the drug a single transduodenal intubation of 25 cc. of a 1 per cent solution of gentian violet medicinal is frequently sufficient to eradicate the parasitic females, particularly those which are deeply embedded in the mucosa. The patient omits breakfast on the morning of treatment, the duodenal tube is placed in position under a fluoroscope and the patient is required to lie down for an hour before intubation, during, and for two hours after intubation. The tube is removed carefully about one hour after treatment. If any of the solution is carried back into the stomach, vomiting may be expected but this does not appreciably interfere with the effect of the drug. A check on these cases for several months after treatment has shown several to be negative. By this technic the upper levels of the small bowel are deeply and adequately stained by the dye and thus a lethal dose of the therapeutic for the parasites is provided (Faust, 1938).

For refractory cases and for those with *Strongyloides* infection of the bronchial epithelium, it is feasible to introduce by vein a one-half per cent solution of the dye, made up in distilled water and filtered. Amounts of [illegible]

remains hospitalized during the period of treatment (Faust and Yao, [illegible]). Physicians are advised not to use solutions more concentrated than 0.5 per cent, or in amounts larger than 20 to 25 cc., or to give the therapeutic more frequently than every other day.

Tests in the author's laboratory on experimentally infected dogs have demonstrated that, when gentian violet reaches the parasitic female worms in sufficient concentration, it invariably kills the worms by combining with their cytoplasm. With enteric-coated pills the difficulty lies in the fact that the coating may not dissolve soon enough to reach the greatest focus of infection in the duodenum; or the dye may penetrate only through the outer portion of the villi and not reach the worms down below the glandular crypts or in the stroma of the glands.

Most patients tolerate the enteric-coated tablets of gentian violet, but some complain of nausea or colicky pains in the pit of the stomach. Experimental dogs show some hyperemia of the intestinal mucosa after administration of the dye in solution, and even in enteric-coated tablets if it is preceded by saline purgation and given on an empty stomach. [illegible]

It is recommended that one [illegible] tablets be first administered. [illegible] duodenal intubation of the dye in solution is probably [illegible] procedure.

In a preliminary study on the therapeutic effects of gentian violet on oxyuriasis Wright, Brady and Bozicevich 1938) found that of 122 persons

with treatment completed, 112 or 91.8 per cent were negative following a full course of the dye, as tested by post-treatment swab examinations. This was confirmed by D'Antoni and Sawitz (1940) and has become standard treatment for oxyuriasis. The preferred method of administration of the drug is as follows:

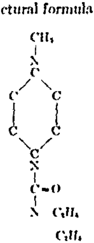
The drug, in four-hour (Seal-Ins or Enseals) enteric coated tablets, is taken three times a day before meals. For an adult, two ½-grain (0.03 Gm.) tablets (*i. e.*, 3 grains or 0.18 Gm. *per diem*) are prescribed; for children, 1 cgm. *per diem* for each year of apparent (not chronological) age. After eight days, the patient is allowed to rest for one week and then takes an additional eight-day treatment.

During a course of oral administration of gentian violet medicinal in one-and-one-half-hr. or four-hour coated tablets nausea and vomiting may be anticipated at least once or twice. Only when the patient vomits the drug on several successive administrations, or develops acute intestinal colic, should the course of treatment be at least temporarily interrupted or discontinued.

VI. Piperazine Compounds

One synthetic compound of this series, which has been screened pharmacologically and tested in experimental animals for its anthelmintic properties, has reached the stage of clinical trial. It is 1-diethyl carbamyl-4-methyl piperazine hydrochloride, or "*Hetrazan*."

Hetrazan.—This is a colorless, crystalline substance which is highly soluble in water. In a one per cent solution it has a pH of 4.1. Its molecular weight is 231.6 and its structural formula is as follows:



Hetrazan is stated to be non-irritating, caused no local anesthesia, no ophthalmia, no effect on blood sugars. Its effect on blood pressure is similar to that of epinephrine. It is eliminated principally by the kidneys, mostly in an unchanged state. In experimental animals toxic doses, considerably below the lethal dose, at times produced nausea, vomiting, shivering and tonic convulsions.

Hetrazan apparently has no effect against most intestinal helminths and *Schistosoma mansoni*. However, it is very effective in filaria infections, including Bancroft's filariasis and onchocercosis.

Santiago-Stevenson, Olivér González and Hewitt (1947) have reported on 26 clinical trials in *Wuchereria bancrofti* in Puerto Rico. Twenty three of this number were symptomless cases. The drug was administered orally three times daily for three to twenty-one days, in amounts totaling 0.5 to 2.0 Gm. per kilo of body weight. The treatment was relatively well tolerated in every case, but fever, headache, nausea, lumbar pain, adenopathy, rash and other allergic manifestations were encountered. There was a marked reduction in circulating microfilariæ and in 13 patients examination for microfilariæ became negative between the ninth and eighty-third day after beginning treatment. In only one patient was the treatment considered to be ineffective. In British Guiana Kenny and Hewitt, in the treatment of 239 cases of Bancroft's filariasis, have provided additional evidence of the specificity of Hetrazan for this infection.

In Mexico (Mazzotti and Hewitt, 1948) and then in Guatemala Hetrazan has been tested on onchocercosis since 1947. The earlier dosages (1 to 2 mgm. per kilo of body weight), based on the Puerto Rican studies on Bancroft's filariasis, were necessarily reduced because of serious side effects. Even with a considerably lower dosage an almost intolerable pruritus developed, as well as edema, weakness, fever, and, in one patient with ocular complications due to the disease, temporary blindness. There is evidence that in onchocercosis Hetrazan is filaricidal but it is problematical if patients can tolerate a sufficient amount of the drug to be effective.

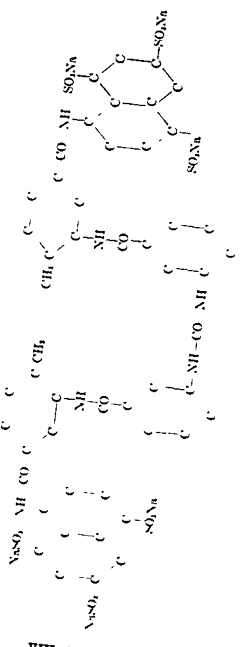
VII. Sulfonic Acid Derivatives

A considerable number of non-metallic sulfonic acid derivatives have been synthesized by German and French chemists for testing against *Trypanosoma gambiense* and *T. rhodesiense*, the organisms producing African trypanosomiasis in man. The earlier efforts produced trypan red and trypan blue. In 1924 Heymann in Germany and Fourneau in France synthesized a complicated chemical compound of molecular weight 1448 (Oesterlin, 1939) or 1428.7 (Merck Index, 1940), which has come to be known under a variety of names, viz., Bayer 205, Fourneau 309, germanin, moranyl, antrypol, naphuride, naganol, suramin, belganyl, etc.

Naphuride Sodium (Germanin, Bayer 205, Fourneau 309).—This is a white powder, which is thermostable and is freely soluble in water, although it requires vigorous shaking to get it in solution. According to Oesterlin (*l. c.*, p. 150) the molecule of Bayer 205 consists of 2-naphthylaminosulfonic acid, 2-aminobenzoic acid and 2-methylaminobenzoic acid, and the structural formula is on following page.

This drug has been found to be very effective in the treatment of both human types of African trypanosomiasis during the acute stage. It is administered intravenously as a 10 per cent solution, in doses of 1 Gm. per week for ten weeks

Clinical trials of naphuride sodium in the treatment of Bancroft's filariasis in Puerto Rico and onchocercosis in Guatemala provide considerable evidence of the specificity of this drug in these two types of filariasis, although considerable discomfort was experienced by the patients during the course of treatment.



The Structural Formula of Naphuride Sodium

VIII Alkaloids

These are tertiary aromatic bases containing carbon, hydrogen and nitrogen and usually also oxygen, are crystalline and usually non-volatile. Of the many alkaloids employed as therapeutic agents the following have demonstrated anthelmintic properties: *emetine*, the principal alkaloid in ipecachuana, *pelletierin*, from the pomegranate, *Punica granatum*, *arecoline*, from the areca or betelnut, *margosine*, from *Melia azadirachta*, *spigeline*, from *Spigelia marylandica*, and *pyrethrine*, from the root of *Anacyclus pyrethrum* (Family Compositae). The first three are clinically in use.

Emetine Hydrochloride.—Emetine, which was discovered by Pelletier and Caventou, in 1817, is insoluble in water. The hydrochloride, a white, odorless, crystalline powder which becomes yellowish on exposure to light, is highly soluble in water. As a 6 per cent solution in water (*i. e.*, 0.06 Gm. in 1 cc.) it is available in sealed ampules. While its greatest use is in the treatment of amebiasis of the liver, it has demonstrated anthelmintic value in fascioliasis (*vide supra*, p. 178) and paragonimiasis (*vide supra*, p. 242), but its usefulness in schistosomiasis is questionable. When administered in Enseals capsules by mouth Burrows, Morehouse and Freed (1947) found emetine hydrochloride to be highly efficient in removing *Trichocephalus* from mental patients but it produced severe intestinal irritation.

Pelletierin.—This anthelmintic principle has been used since the days of the Egyptian Middle Kingdom for removing *Tænia saginata* and even today has considerable popularity. Pelletierin tannate, pelletierin sulfate and pelletierin hydrochloride are all employed, but the first mentioned is preferred by American physicians because of its lower toxicity. The therapeutic product is "a mixture of the tannates of the several alkaloids obtained from pomegranate, *Punica granatum*" (U. S. P. XI, p. 278).

Pelletierin tannate is a tasteless, hygroscopic, yellowish powder, only sparingly soluble in water. [illegible] stomach in an amount not [illegible] is followed within two hours by a saline purgative. [illegible] (1929) it has only a 35 per cent efficiency in removing the entire worm. It is believed to be especially satisfactory for *Tænia solium* but is ineffective in removing *Hymenolepis nana*. In therapeutic doses it causes colicky diarrhea, headache, vertigo, drowsiness, and at times vomiting and diplopia. Medication in excess of the indicated dosage may result in weakness, ascending paralysis and temporary blindness. The therapeutic dose and method of administration of the hydrochloride are similar to the tannate. No alcohol should be permitted for forty-eight hours preceding treatment and for twenty-four hours afterwards.

The sulfate is popularly prescribed in a preparation known as *Tanret's pelletierin*, which contains, in addition, extract of catechu (pelletierin sulfate, 0.25 Gm.; extract of catechu, 1.0 Gm.; syrup of bitter orange peel, 25 cc.; aq. dist., 10 cc.). It is followed in one-half hour by 1 to 2 ounces of castor oil. This preparation is very expensive and deteriorates rapidly in the Tropics.

Infusion of fresh pomegranate bark may be prepared by macerating 50 grams in 750 cc. of water for twenty-four hours and allowing to evaporate to 200 cc. The full dose is taken on an empty stomach and is followed within an hour by a purgative. The dose for children is one-half that for an adult (Stitt, 1929).

The use of [illegible] in pregnancy.

Areca (Bete [illegible] 136) betel nut has been used in China for tæniasis for about [illegible]. These nuts are the seeds of *Areca catechu*, which is cultivated in Southern India and the Far East. Their effective principle is the alkaloid arecoline ($C_8H_{13}NO_2$), which acts much like pilocarpine. A decoction is made of 30 grams (1 ounce) of the dried powder or shavings of the nut (obtainable in Oriental pharmacies) in

200 cc. (6½ ounces) of distilled water. The mixture is boiled for thirty minutes over a water bath. The patient is advised to eat only light food for a day or two before treatment but needs no catharsis unless he is constipated. The decoction is taken in the morning on a fasting stomach and food is proscribed for six hours. A bowel movement, containing the worm, may be anticipated one to three hours after treatment, without purgation. In case the head is not obtained, Liu (loc. cit.) recommends an enema of the decoction half strength. In 10 cases treated with betel nut this physician expelled 15 tapeworms, of which 10 were *Tænia saginata*, 2 *T. solium* and 3 not designated. Of the total number recovered 10 possessed heads. There was no recurrence of infection in these cases one and a half to two and a half years later. One patient who passed a worm without a head was negative six months later.

This prescription is stated to be cheap, essentially non-toxic in doses of 30 grams of the dried nut and is believed to be successful when other tænifuges have been inefficient.

IX. Antimony Compounds

In 1918 Christopherson first used antimony for cases of schistosomiasis. Both tartar emetic (potassium antimonyl tartrate) and sodium antimonyl tartrate, as well as colloidal antimony preparations, were found by physicians in endemic areas to be valuable specifics for all three types of blood fluke infection. In the earlier preparations there is evidence that the drug administered was actually a combination of antimony tartrate with potassium *and* sodium. Tartar emetic is the most stable and cheapest of these preparations but has been found to be somewhat more toxic. All of these preparations require intravenous administration and great care must be exercised not to introduce any of the solution into the perivascular tissues lest necrosis occur. More recently anthiomaline and other antimony compounds have been tested not only in schistosomiasis but in filariasis.

Tartar emetic (Potassium antimonyl tartrate).—This is a colorless, odorless, crystal or powder which is readily soluble in water and is stable in aqueous solution. It contains 36.47 per cent Sb and is 99 to 99.7 per cent pure in commercial form. The structural formula is,

$$K\ OOC\ CHOH\ CHOH\ COO(SbO)\ \tfrac{1}{2}H_2O$$

In aqueous solution tartar emetic is irritating to perivascular tissues, the bronchial epithelium and the liver parenchyma. When administered therapeutically ([illegible]
bly vomiting. I [illegible]
amounts can be [illegible]
excreted in the urine and the feces (Bartter *et al.* 1917).

This was the first drug found to be effective in the treatment of schistosomiasis (Christopherson, 1918), and is probably the most reliable for this purpose. Although a 6 per cent solution is fairly well tolerated in schistosomiasis hæmatobia, for intestinal schistosomiasis, because of liver involvement, a ½ or, at most, 1 per cent solution is indicated. It is administered intravenously on alternate days or three times weekly until at least 3.50 cc. of the ½ per cent solution, containing 0.576 Gm. of Sb, have been

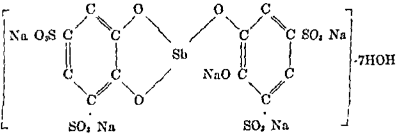
given. This provides up to 84 per cent cure in schistosomiasis japonica, the most serious type and the one most difficult to eradicate. For details of use in the three human types of schistosomiasis *vide supra*, pp. *119, 137* and 157.

Sodium Antimonyl Tartrate.—This double salt has physical characteristics rather similar to tartar emetic. Its structural formula is:

Na OOC CHOH CHOH COO(SbO) $\frac{1}{2}$HOH

In aqueous solution it is unstable and for therapeutic use it must be prepared fresh each time before administration. Like tartar emetic it must be given by the intravenous route. It is reported to be much better tolerated than tartar emetic but its instability, particularly in warm climates, is a serious handicap to its common use. It probably has as high a cure rate as tartar emetic in schistosomiasis when a comparable amount of metallic Sb has been employed in a course of treatment. Shattuck (1924) recorded satisfactory results with this drug in clonorchiasis. (*Vide supra*, p. *221.*)

Fuadin (Sodium antimonyl III bis-catechol-2, 4 disulfonate; stibophen or neoantimosan).—This antimonial is a colorless, odorless, crystal or powder which is readily soluble in water and contains 13.6 of trivalent Sb. Its structural formula is as follows:



Fuadin was synthesized in Germany particularly for use in schistosomiasis. The drug is made up as a 6 to 7 per cent aqueous solution. (A 6 per cent solution contains 8.5 mgm. Sb. per ml.) Reports of the first clinical tests were made by *Khalil, Nami, Peter, El Din and Betache* (1929). Because it is administered intramuscularly rather than intravenously and produces relatively minimal local and systemic reaction, it has distinct advantages over tartar emetic. In 1930 Khalil and Betache reported 97.9 per cent cures in 2041 cases in Egypt. By 1936 Khalil modified his earlier findings as follows: 9 injections totaling 40 cc. solution produced 53 per cent cures; 11 inje[illegible]
with 60 cc., 80.6 per cen[illegible]
cent remained infected. [illegible]
reported only about 50 per cent apparent cures in schistosomiasis japonica.

[illegible] of 45 cc. each is not very [illegible]
[illegible] examinations). Meira (1946)
[illegible] of hepato-splenomegaly due to schistosomiasis but is contraindicated in patients with renal and cardiac lesions.

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15 patients free of microfilariæ following a full course of treatment.

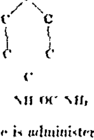
Anthiomaline (Lithium antimonyl thiomalate).—This antimony salt was synthesized by French chemists for trial against African trypanosomiasis. It is a colorless, odorless, crystal or powder, readily soluble in water but relatively unstable in solution. It contains about 15 per cent trivalent Sb. The structural formula is as follows:

$$\left[\begin{array}{l}\mathrm{Li{-}OOC{-}CH{-}S}\\ \mathrm{Li{-}OOC{-}CH_2}\end{array}\right]^{\bullet}\cdot\mathrm{Sb\ 9HOH}$$

This drug is made up as a 16 per cent aqueous solution for intramuscular injection; each ml. contains 0.06 Gm. of the salt or about 10 mgm. Sb.

Earlier reports of the effectiveness of anthiomaline in the treatment of schistosomiasis in Africa (Montestruc and Bertrand, 1936; Moulinard, 1936, Ashkar, 1938, and Bauge, 1941) indicated that the drug was well tolerated when given intramuscularly and was as frequently curative as tartar emetic and fuadin. Subsequent tests, both in the laboratory and clinically, have failed to justify any enthusiastic claims for this drug in schistosomiasis or Bancroft's filariasis. Brown (1944) obtained 85 to 100 per cent temporary reduction in microfilarial counts in patients harboring *Wuchereria bancrofti* for four to five months following a full course of treatment with this drug, but Culbertson *et al.*, (1947) reported only 7 of 20 patients free of microfilariæ.

Urea Stibamine.—This pentavalent ammonium salt of carbamino-phenylstibinic acid was synthesized by Brahmachari in 1920, in India, for the treatment of kala-azar, and has proven to be one of the most valuable drugs for this purpose. It is a buff-colored powder, fairly soluble in water and contains about 35 per cent metallic Sb. The structural formula is stated to be (Oesterlin, 1939, p. 218):

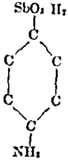


In kala-azar urea stibamine is administered intravenously as a 5 to 10 per cent solution, in increasing daily amounts beginning with 1 cc. and reaching 4 cc. until 12 to 18 cc. containing 1.2 to 1.8 Gm. of the salt have been given. The drug is fairly well tolerated but the solution must be prepared freshly before each administration.

In clinical trial in 11 cases of schistosomiasis mansoni Hernández-Morales *et al.*, (1946) administered this drug three times daily under hospital supervision up to a total maximum tolerance of 3.4 to 10.125 Gm. of the salt (average for male patients, 7.18 Gm. over 16 days, for female

patients, 6.69 Gm. over 13 days). Considerable toxicity was demonstrated and one patient died as a result of the treatment. Twelve of the 13 surviving patients were free of eggs in the stools up to 4 months following treatment. In four of six cases of Bancrofts' filariasis Culbertson *et al.*, (1947) obtained microfilaria-free blood 16 months following administration of 3.3 to 7.1 Gm. of the drug.

Neostibosan (Heyden 693b).—This pentavalent ammonium salt of *p*-aminophenylstibinic acid was synthesized by Heyden in Germany in an attempt to obtain a more stable compound than stibosan (3-chlor-4 acetamino-phenylstibinic acid or Heyden 693). It is potent and is the most satisfactory single drug for treatment of kala-azar. Moreover, it may be administered intramuscularly as well as intravenously, usually as a 5 per cent solution. This drug is a pinkish-buff powder which is moderately soluble in water. It contains 42.0 per cent metallic Sb. The structural formula is as follows:



Culbertson *et al.*, (1947) employed neostibosan in the treatment of 35 cases of Bancroft's filariasis, 3 cases (father, mother and young daughter) with loaiasis, and 40 cases of onchocercosis (7 of which were followed up for ten months and one for five months). In *W. bancrofti* infection the average treatment consisted of 6 to 9 Gm. of the drug in a period of thirty-three to fifty-eight days. Fifteen of a group of 20 patients examined twenty-four months following treatment were free of microfilariæ; 7 of 10 others followed for fourteen months were similarly negative, and 3 of the 5 others followed for sixteen months were negative. In one of the three cases of loaisis with demonstrable microfilariæ in the blood preceding treatment the number became greatly reduced following administration of 16.4 Gm. of the drug. In none of the *Onchocerca* infections was sterilization accomplished with respect to microfilariæ in the skin. Among the antimonials thus far tested in Bancroft's filariasis Culbertson *et al.*, (*l. c.*) regard neostibosan as most effective.

Other Antimony Compounds.—Culbertson *et al.*, (1947) made clinical tests of two other pentavalent antimonials on Bancroft's filariasis. Using *neostam (rel* stibamine glucoside) and *stibanose*, 5 of 11 cases became microfilariæ-free when the former drug was employed (2 1 to 11.4 Gm) and one of 5 when the latter was used (13.8 to 15.2 Gm.).

X. Arsenicals

Melarsen Oxide.—This drug was employed by Culbertson *et al.*, (1947) in the treatment of 18 cases of Bancroft's filariasis In 3 instances the drug

was administered by mouth in 50 mgm. capsules three times daily for eight to fourteen days (total drug, 1.05 to 1.5 Gm.). The remaining 15 patients received the drug dissolved in propylene glycol by the intravenous route for seven to nine days (total drug, 60 to 90 mgm.). One of the former group and six of the latter were microfilaria-free from seven to thirteen months following treatment Severe toxic symptoms resulted in some of the intravenously treated individuals.

XI. Proteolytic Enzymes

Certain proteolytic enzymes obtained from plants have demonstrated anthelmintic activity. Those which have been studied particularly are *bromelin*, in the juice of the pineapple, *Ananassa sativa* (Asenjo, 1939, 1940), *papain*, in the juice of the papaya, *Carica papaya* (Hassler, 1928 and Asenjo, 1941) and *ficin*, in the milky juice of *Ficus glabrata* and other species of the fig family (Bayon, 1771; Berrio, 1911; Caldwell and Caldwell, 1929; Robbins, 1930, Thomen, 1939, and Faust and Thomen, 1941). The last of these three has nearly two centuries of demonstrated usefulness.

Leche de Higuerón (Higuerolatex).—For many years the crude sap of two of the bastard fig trees (*Ficus glabrata*, syn *F. laurifolia*) and *F doliaria* in Central and Northern South America has been recognized to be an efficient anthelmintic and has been found to be especially lethal to whipworms This sap, locally known as *leche de higuerón*, *higuerolatex* or *doliaria*, is a whitish, creamy, viscous substance, with a slightly acid but not unpleasant taste. Other trees of the genus *Ficus* contain sap having the anthelmintic fraction, but only the species *F glabrata* and *F doliaria* are known to contain it in efficient quantities. The effective principle is an enzyme, known as *ficin* (Robbins, 1930), is considerably more potent than papain, and is apparently harmless to the normal intestinal wall when administered in the form of crude sap. Unfortunately the untreated *leche* ferments rapidly unless kept cool in the refrigerator. The Colombian *leche de higuerón* is preserved by adding 1 per cent sodium benzoate to the crude sap It is available in certain Latin-American countries, where it is sold under the trade name Higueroma. Samples of this commercial product, tested in the present author's laboratory, have assayed about 75 per cent efficient when compared with the refrigerated unpreserved *leche*.

Caldwell and Caldwell (1929) tested the crude refrigerated *leche de higuerón* in a series of *Trichocephalus* cases in Alabama and rated it 85 per cent efficient in removal of the worms. Since 1930 the present author has used this product, obtained mostly from Panamanian sources, and has found it much more efficient as a trichocephalicide than any other available preparation The therapeutic dose is 2 ounces (60 cc), taken preferably on an empty stomach and washed down with a half glass of water In the author's experience with several hundred clinic cases, no patient, even a small child, has had difficulty in taking the product and no single case has complained of any ill-effects It is most successful if a saline purge (15 grams or ½ ounce in a glass of water) is taken the night before treatment, if food is omitted the morning of treatment and if a saline purge is taken two to four hours after the *leche* has been administered Meira (1946) states that fresh leche de higuerón is incapable of eradicating *Strongyloides*

stercoralis, *Tænia* spp. or *Hymenolepis nana*. He includes the experience of Romeu Cançado that it is very effective against hookworms, *Trichocephalus* and *Ascaris*, and that it may be administered orally in 30 to 60 cc. amounts or by transduodenal tube in 15 to 25 cc. amounts.

XII. Miscellaneous Anthelmintics

Kousso.—The natives of Ethiopia eat the flowers of kousso (*Brayera anthelmintica*) in order to evacuate *Tænia saginata*. It has a disagreeable taste, is extremely irritating to the intestinal mucosa and is very high-priced. Moreover, there is little or no evidence that the heads of the worms are expelled.

Pumpkin Seed.—A household remedy for tapeworms in many countries consists in crushing to a paste one to three ounces and ingesting the whole seed of cucurbitaceous plants, usually those of the pumpkin, occasionally of the watermelon. Krayer (1937) has studied the efficacy of pumpkin seed therapy employed in Lebanon and strongly recommends it as a safe and satisfactory procedure. For a course of treatment he utilizes 400 to 700 grams of the seeds for an adult, 200 to 400 grams for a child. The seeds are thoroughly mashed and are mixed with honey or fruit syrup or, preferably, are made into an aqueous decoction. To prepare the decoction, unhulled small seeds are placed in twice their volume of water, are heated to the boiling point and strained through a cloth. The electuary or the extract is taken on an empty stomach without the necessity of pre-treatment purgation, but it should be followed by a saline cathartic, since it does not in itself kill the worms and is not hydragogic. Contrary to common belief, Krayer (loc. cit.) states that the effective principle in pumpkin seed is not in the oily resin but in a heat-resistant fraction in the aqueous extract. Neveu-Lemaire (1936) states that pumpkin seed is an entirely safe prescription in pregnancy.

Quassia.—This is obtained from the Surinam *Quassia amara* but more commonly from the Jamaican species, *Q. excelsa*. An infusion is made of the powdered trunk or branch wood. Two ounces of the powder are placed in a pint of boiling water and the mixture is left to stand for twelve hours. On each of three successive mornings the tapeworm patient takes 5 ounces of the infusion with ½ ounce of Epsom salts. The worm is almost always expelled without the head.

Coconut.—This is an old native remedy of India and the West Indies for tapeworms. The patient fasts and on each of several mornings takes the ground meat and milk of one nut. No purgative is necessary, since the milk has a hydragogic action. In the limited experience of the present author with this therapeutic procedure the greater part of the worm is expelled but the head remains attached and in due course produces a new worm.

Miracil.—This chemical compound (*1-methyl-4-diethylaminoethylamino-*thioxanthone) was synthesized by Mauss and has been found by Kikuth and Gönnert to show activity against *Schistosoma mansoni* in experimental mice. Single doses of 1.0 Gm. per kilo by mouth or 10 doses of 0.125 Gm. are tolerated. The LD_{50} by vein is 0.45 Gm. per kilo. Rabbits are less tolerant by both routes (Wood, 1947).

RECOMMENDATIONS ON ANTHELMINTIC AND SUPPORTIVE MEDICATION

Although experience has demonstrated that mass therapy of large groups of infected persons employed on plantations in the Tropics is feasible, it is assumed that the average physician desiring information on the treatment of helminthic infections is interested in the use of anthelmintics for individual cases, or, at most, for small groups of patients.

Because of the toxicity of practically all specific anthelmintics, before such specifics are administered it is highly desirable not only to have an accurate diagnosis of the infection (which is usually obtained by fecal and blood examination for parasites), but also to have made a careful physical examination of the patient. It is also important to have a rather complete blood picture, including a total erythrocyte count and both a total and differential white cell count, as well as a relatively accurate hemoglobin estimation. If facilities are available, this latter estimate should be made by the Newcomer hemoglobinometer rather than by the Tallqvist scale which is notoriously inaccurate. If there is a significant anemia, iron salts or, at times, also liver extract are indicated as a pre-treatment precaution, and, in cases of extreme anemia, one or more transfusions of whole blood may be required before specific therapy is instituted. Likewise, no treatment should be administered to a patient suffering from acute nephritis, acute cardiac, pulmonary, [illegible] fever. Especial caution [illegible] cirrhosis of the liver, acu[illegible] pregnancies In cases suggesting hypoglycemia, calcium gluconate or calcium lactate may be administered prophylactically for several days in advance of specific treatment.

For oral administration of vermicides, in all intestinal helminthiases except strongyloidiasis and in patients who are dehydrated or have severe diarrhea, saline purgation the night before treatment is advised, in order to free the bowel of food and fecal material, so that the drug, when administered, may act promptly on the worms. Glauber salts (sodium sulfate) is preferred to Epsom salts (magnesium sulfate), since the former not only dissolves mucus from the crypts and folds of the mucosal surface of the bowel wall (and thus permits the drug to come in immediate contact with the heads of attached worms), but also has no toxic ions to be absorbed by the blood stream The somewhat nauseating taste of Glauber salts may be concealed by the addition to it of fresh lemon or lime juice.

Most anthelmintics are administered on an empty stomach. If the drug is especially toxic (*i. e.*, carbon tetrachloride, oil of chenopodium, *oleoresin of male fern, etc.*), it is desirable that the patient be hospitalized on the day of treatment and be made as quiet and comfortable as possible just before administration of the drug. For intubation of a drug, as in the administration of a solution of gentian violet medicinal, an emulsion containing the oleoresin of Aspidium or crude leche de higuerón, the patient should be allowed to relax for at least a half hour before the duodenal tube is introduced After it has been satisfactorily placed another short period of rest should be allowed. Then the anthelmintic should be rather slowly installed,

following which the patient should be kept quiet again for a short while before the tube is withdrawn.

Purgation accompanying the specific anthelmintic for intestinal worms, or shortly after its administration, is quite a necessary part of successful therapy. This is not only to prevent excessive absorption of the drug but also to evacuate dead and dying worms as soon as possible. For most therapeutics saline purgation (*i. e.*, with Glauber or Epsom salts) is indicated in preference to castor oil. Some physicians administer the purgative along with the anthelmintic, in order to save time and trouble, although more successful results are obtained when the saline purgative is given one hour (or preferably two hours) after specific medication.

The patient will normally have one or more copious bowel movements within two hours after post-treatment purgation. In case at least one adequate evacuation has not been obtained within a four-hour period, a high, tepid water enema should be administered. For several hours after therapeusis it is desirable to collect and examine the entire stools for discharged worms, in order to obtain evidence of the success of the treatment

Food is permitted only after the post-treatment purgation has been effective in cleaning out the bowel. For the first meal or two after treatment a relatively bland diet is recommended.

After anthelmintic medication for roundworm and fluke infections of the intestines, follow-up stool examination should be made not earlier than four days later. If the feces are examined at an earlier time they may contain eggs of disintegrating worms which were not evacuated at the time of treatment. In tapeworm infections, even though the greater part of the worm has been discharged, if the head and neck remain attached to the patient's intestinal wall, a complete new worm will usually regenerate in ten days (dwarf tapeworm) to several months (beef and pork tapeworms) Hence, previous to these respective times the feces may be negative and yet the infection may not have been removed.

In case one treatment for an intestinal roundworm or fluke infection has not been successful in removing all of the worms, as determined by post-treatment examination of the feces, it is usually desirable to wait at least one week or ten days before undertaking a second course of treatment. For tapeworm infections, re-treatment is feasible as soon as helminthological evidence of the infection reappears, but on the average should not be attempted until such concrete evidence is available. Evaluation of the success of treatment for the elimination of blood flukes (schistosomes) or fluke infections of the biliary tracts (*i. e.*, *Clonorchis, Opisthorchis, Fasciola*) or lungs (*Paragonimus*) requires repeated examination of the excreta in which the eggs are discharged. Not less than six months and preferably twelve months, employing the most efficient concentration technics, are required before negative findings may be regarded as significant. Similarly, in filaria infections post-treatment examinations for microfilariæ should be made periodically for many months before the patient can be regarded as freed of the infection. Claims of "cures" have all too frequently been based [illegible] of an

Helminthologists utilize tw[illegible] per-
anthelmintic. One is the "*worm removal rate*" [illegible]

centage of worms in a given infection removed by a course of treatment. The other is the "*cure rate*" and is based on the average percentage of cases treated in which complete worm removal has been effected by a course of treatment. Thus, if the patient harbored 100 hookworms and a single course of an anthelmintic procedure removed 75 of these worms, the *worm removal rate* in that case is 75 per cent but the *cure rate* is 0 per cent. On the other hand, if specific treatment of 100 patients harboring hookworms resulted in complete eradication in 75 cases the *cure rate* is 75 per cent.

A careful distinction must be made between *helminthic infection* and *helminthic disease*. The former is merely an indication of the presence of the worm and does not necessarily mean that the patient is suffering from the infection. Thus, a small number of hookworms or whipworms (25 or fewer) does not usually evoke symptoms, although in susceptible individuals, particularly children, this number may produce clinical manifestations. On the other hand, a single *Ascaris* may set up grave local or systemic reactions. While it is desirable to eliminate all of the worms in a particular infection, this may be impracticable.

In the warmer climates and in the Orient multiple helminthic infections are quite common. Thus, ascariasis may be complicated by whipworm and hookworm infection, and in children by oxyuriasis or dwarf tapeworm infection. Or hookworm disease may be associated with strongyloidiasis. Likewise, one or more helminthiases may be complicated by amebiasis (*i. e.*, infection with *Endamœba histolytica*). In mixed infections, after diagnosis has been obtained, it is first necessary for the physician to obtain a proper evaluation of the respective parasitoses and to determine which infection is producing the greater pathology. Specific therapy should then be directed first to the elimination of this infection, to be followed by other therapeutic procedures to remove the remaining infections. Although a single anthelmintic may be effective against two or three species of parasites, there is no *one drug which is useful as a general anthelmintic, and rarely is one drug* equally efficient in destroying two different species of worms.

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